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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 34 NOVEMBER, 1953 No. 5

Original Communications

THE USE OF CELLULOSE SPONGES IN SURGERY

A PRELIMINARY REPORT

JOHN R. PAINE, M.D., AND RICHARD W. EGAN, M.D., BUFFALO, N. Y.

(From the Department of Surgery, Buffalo General Hospital, and University of Buffalo School of Medicine)

INTRODUCTION

RECENTLY a series of studies was begun at the Buffalo General Hospital to evaluate the use of manufactured cellulose sponges* as a substitute for the usual cotton gauze sponges and packs used in the performance of surgical operations. These studies have been carried out in both the experimental surgical laboratory and the operating rooms. Although these studies are to be continued, the preliminary results have so clearly indicated certain important advantages of the cellulose sponge that it seems proper to call the attention of members of the profession to the potentialities of this new product.

This sponge material is manufactured primarily from cellulose recovered from wood by means of standard industrial chemical processes. These processes entail dissolving the cellulose by means of sodium hydroxide and carbon disulfide and then extruding it through a special orifice to give the size, shape, and thickness of the finished product desired. Flecks of barium sulfate are incorporated in the liquid stage of the sponge material to provide an evenly distributed characteristic radiopaque pattern. By minor variations in the manufacturing process, certain of the physical characteristics of the sponge may be altered within fairly wide limits as desired.

PHYSICAL CHARACTERISTICS OF THE SPONGE

The cellulose sponges which we have used have been 1 mm. in thickness and four by eight inches in size in the dry state. When moistened, the sponges become approximately 3 mm. in thickness. The tensile strength of this product is approximately ninety pounds per square inch, and it has an average density (grams per cubic centimeter) of 0.2 to 0.3. The average weight of such a sponge four by eight inches in size is 8.86 Gm. in the dry state; the total absorption

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*This material may be obtained from the O-Cel-O Division of General Mills, Inc., Buffalo, N. Y.

of water by weight is 1,100 to 1,300 per cent in the dry state. In clinical use, however, the sponges have been used after first being wet and then wrung out, as only in the moistened state is the material sufficiently soft and flexible. Comparative absorption tests using oxalated bovine blood warmed to room temperature have given the following results:

	COTTON GAUZE SPONGE (DRY)	CELLULOSE SPONGE (MOIST)
Total absorption by weight	503 per cent	973 per cent
Wetting time	4.5 seconds	1.8 seconds
Rate of absorption (inches per second)	0.89	2.29

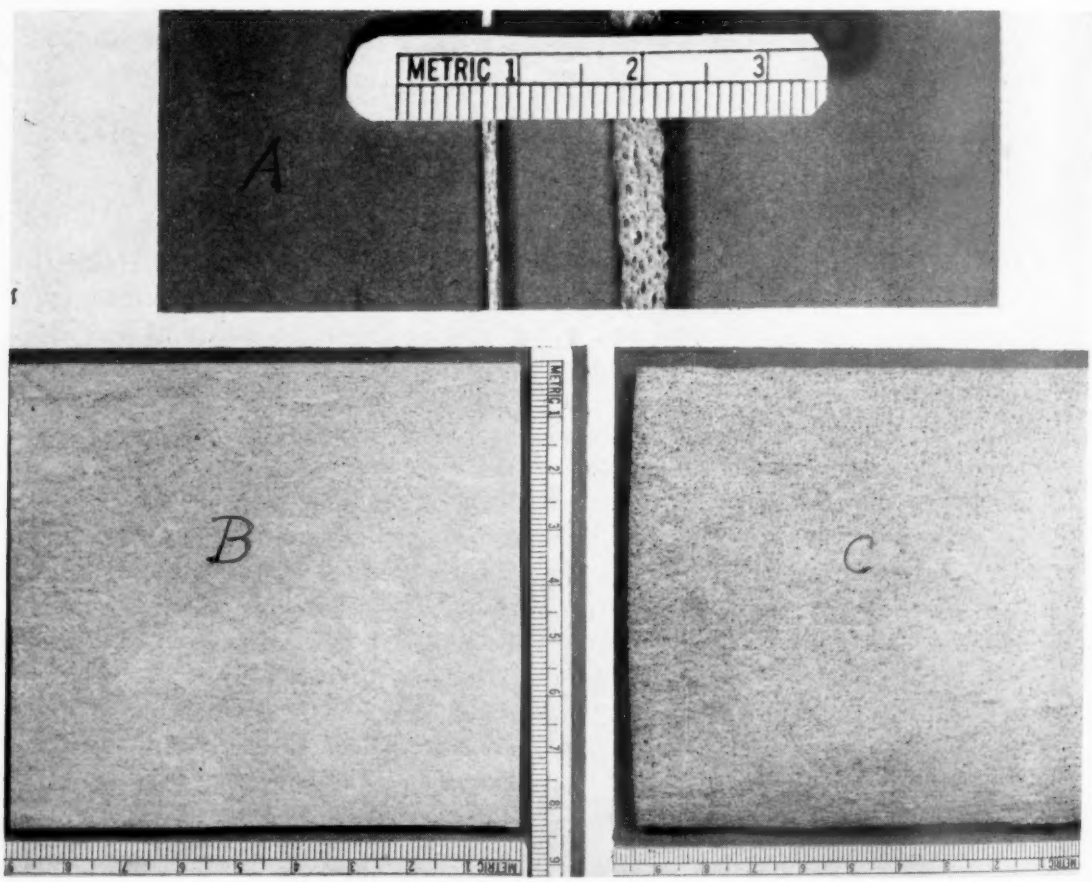

Fig. 1.—The cellulose surgical sponge. *A*, Cross sections of the sponge in the dry state (left) and when moistened (right); *B*, cellulose sponge four inches square in dry state; *C*, cellulose sponge four inches square when moistened. The slight increase in size of this material when moistened is evident.

It is, therefore, obvious that the absorbent ability of the cellulose surgical sponge when moistened is approximately twice that of the cotton gauze sponge of the same size when dry. The wetting time and rate of absorption of the dampened cellulose sponge are far superior for surgical purposes than the same properties of dry gauze.

ANIMAL EXPERIMENTS

Prior to using this material in the operating room, its effect on living tissues was tested by implanting portions of it in various locations in dogs.

The material to be tested was first thoroughly washed in tap water and then autoclaved for thirty minutes at 250° F. Two healthy mongrel dogs were used. Nembutal solution injected intravenously was used for anesthesia, and all operative procedures were performed with aseptic technique.

Dog 1.—Portions of the sponge 1 to 2 cm. square were placed: (a) beneath the peritoneum in immediate contact with the iliac vessels, (b) scattered free in the peritoneal cavity, and (c) wrapped in omentum.

The abdomen was closed in layers with cotton sutures without drainage. Eight days later a right thoracotomy was performed, and 1 to 2 cm. square portions of the sponge were placed: (a) within the pericardium in contact with the ventricles of the heart, (b) beneath the pleura between the artery and vein of the right middle lobe of the lung, (c) on the superior surface of the diaphragm, (d) within the mediastinum, and (e) in the subcutaneous tissues of the chest wall.

The thoracic-wall incision was closed in layers with cotton sutures without drainage.

Dog 2.—Portions of the sponge material 1 to 2 cm. square were placed: (a) within the pericardial sac, (b) within the hilus of the right lung, (c) beneath the pleura adjacent to the esophagus, (d) on the superior surface of the diaphragm, (e) in the apex of the pleural cavity, (f) wrapped in the omentum, (g) beneath the peritoneum in the left upper quadrant of the abdomen, and (h) in the subcutaneous tissues of the abdominal wall.

Both animals recovered from the operative procedures without complications. There was no evidence of infection, toxicity, or limitation of normal activity. Dog 1 was sacrificed thirty days following the second operation, and Dog 2 was sacrificed after seventy days. In both animals the post-mortem findings were similar. There was a moderate inflammatory reaction with loose fibrous adhesions involving the surrounding structures in the immediate vicinity of the implanted material.

Photomicrographs of the implanted material and surrounding tissues removed at the time of sacrifice of the experimental animal show a moderate inflammatory reaction with the usual round-cell infiltration and some foreign-body giant cells. There was a distinct proliferation of fibroblasts which not only encased the foreign material but invaded all its interstices. (See Figs. 2 and 3.)

Roentgenograms taken of dogs in which portions of the cellulose sponge material have been implanted present a characteristic picture which allows the sponge to be located without difficulty. The dispersion of particles of barium sulfate in the cellulose during the manufacturing process ensures the identification of even a small portion of the sponge should it be inadvertently enclosed in a wound.

CLINICAL USE OF THE CELLULOSE SPONGE

Having shown to our own satisfaction that the reaction of living tissues to the cellulose sponge was at least no greater than that to gauze sponges, this material was used in the operating room. Cellulose sponges 1 mm. thick in the

Fig. 2.—Photomicrograph showing central and marginal portions of the cellulose surgical sponge imbedded for seventy days beneath the pleura and pericardium of a dog. The interstices of the sponge are filled with an edemalike fluid containing leukocytes and macrophages. Giant cells are particularly numerous in the marginal portions of the sponge. Tissues intimately in contact with the sponge show no reaction at all.

dry state and four by eight inches in size were autoclaved in the routine manner, as are the usual gauze sponges, linen, and towels. A basin containing sterile water was provided for the instrument nurse. As the sponges became impregnated with blood, they were rinsed in this water and were returned to the operative field for repeated use. When used in this manner, only a very few sponges are required for any operation; usually no more than four to eight.

Listed in Table I are a few operations in which cellulose sponges have been used, as well as the estimated number of gauze sponges usually required for the same operation.

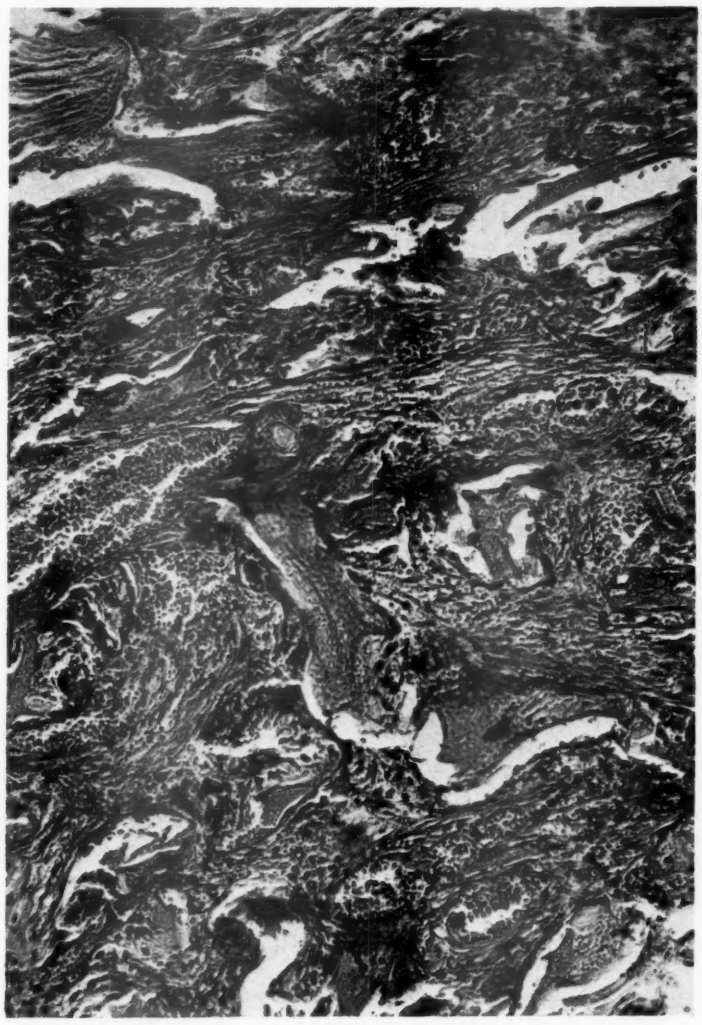

Fig. 3.—Photomicrograph showing a few fibers of the cellulose surgical sponge imbedded for thirty-one days immediately adjacent to the common iliac artery of a dog. The sponge fibers are completely surrounded by a network of fibroblasts and numerous capillaries. An occasional giant cell is seen. The iliac artery showed no tissue reaction at all.

DISCUSSION

At the Buffalo General Hospital, clinical trial of the cellulose sponge has now been made in approximately forty major surgical operations performed by three senior surgeons. A sufficient experience has been obtained to furnish certain definite impressions. In regard to the material now available, these are as follows:

1. The absorptive ability of the sponge is remarkable and increases the ease of securing the small bleeders in the skin and subcutaneous tissues.

2. The pliability of the material is quite satisfactory for operations in which the depth of the incision is not too great.

3. Some difficulty was found in the use of this material in deep small incisions or in narrow crevices due to its thickness and resiliency.

4. The resilience and thickness of the material now available makes it somewhat more difficult to handle small structures and bowel.

5. The tremendously greater absorptive power of the cellulose sponge material as compared to cotton gauze makes it ideal when used as a pack or as protection for the edges of an incision, when used under retractors or a rib spreader.

6. The number of cellulose sponges required per operation is much less than the number of gauze sponges used, since the cellulose sponges can be rinsed out and used repeatedly.

7. The texture of the material is such that its use does not injure delicate structures, although the handling of such structures is more difficult.

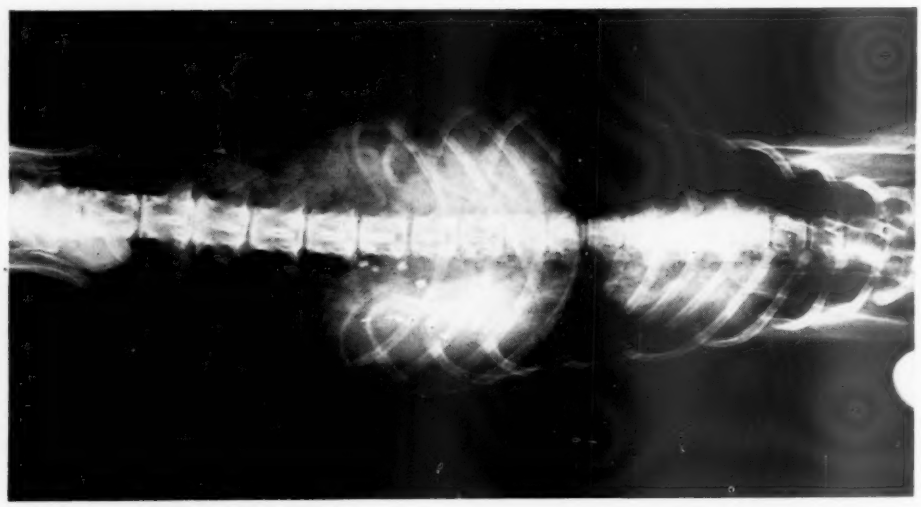

Fig. 4.—Roentgenograph of a dog in the abdomen of which a two-inch-square portion of cellulose surgical sponge had been implanted. The barium sulfate particles incorporated in the material provide a fairly characteristic x-ray pattern.

Some type of sponge manufactured from cellulose would seem to have definite possibilities for use in the performance of surgical operations. There is no reason, however, to expect it to replace gauze sponges entirely In some operations we have found the cellulose product to be entirely adequate; in others, certain parts of the operation seem best conducted using both the gauze and cellulose sponges or just the gauze sponge alone. In any event, the decrease in the total number of sponges required has been striking. The significance of this is twofold. The making of an accurate sponge count at the end of an operation is greatly facilitated and therefore more accurate. For this reason the nurses in our operating rooms are always pleased when the cellulose sponge is used. The cost of sponges, which is a large item in all operating rooms, is much less when cellulose sponges are used. The cellulose sponges now cost but little more than gauze sponges, sponge for sponge.

TABLE I. OPERATIONS PERFORMED AND NUMBER OF SPONGES USED

OPERATION	CELLULOSE SPONGES USED (FOUR × EIGHT INCHES)	GAUZE SPONGES USED (FOUR × EIGHT INCHES)	ESTIMATED GAUZE SPONGES USUALLY REQUIRED (FOUR × EIGHT INCHES)
Exploratory laparotomy	3	3	24
Esophagogastrectomy	8	144	200
Cholecystectomy	3	5	36
Pulmonary lobectomy	5	15	72
Esophagectomy	9	9	120
Inguinal herniorrhaphy	6	0	36
Inguinal herniorrhaphy	6	0	36
Exploratory thoracotomy	6	12	36
Radical mastectomy	6	18	48
Pericardiectomy	2	24	48
Appendectomy	2	2	12

The ability to rinse out a sponge and to use it repeatedly during the course of an operation assumes the maintenance of a sterile field. Cellulose sponges used in that part of an operation when the gastrointestinal tract has been opened or when any contaminated material is encountered of course must be discarded lest all parts of the operative field be contaminated.

As furnished by the manufacturers, the cellulose sponge is quite compressed and can be easily stored in a relatively small space. When wet or autoclaved, however, the material expands somewhat in bulk. Allowance for this must be made in preparing the material for use in the operating room.

The rinsing out of the blood-filled sponges in water for repeated use during an operation, as we have done, should provide an easier and more accurate method of estimating blood loss during an operation than is possible when cotton sponges are used.

SUMMARY

Sponges manufactured from cellulose recovered from wood, and in which flecks of barium sulfate have been incorporated, have been used in a variety of surgical operations at the Buffalo General Hospital as a substitute for the usual surgical gauze sponges.

The reaction of living tissues to this cellulose material has been tested by implanting portions of the sponges in various locations in dogs. The reaction observed has been no greater than that seen with surgical gauze.

Some of the advantages, as well as the limitations, of this new material have been pointed out.

CONCLUSIONS

Sponges manufactured from cellulose from wood have certain definite advantages over the usual gauze spone. The absorptive power of the cellulose material is much greater than that of gauze sponges of comparable size. The ability to rinse out quickly the blood-impregnated cellulose sponge and to use it repeatedly during an operation leads to a decrease in the number of sponges required and makes sponge counts at the completion of an operation quicker and more accurate. Less storage space is required and costs are decreased.

INFLAMMATORY CARCINOMA OF THE BREAST IN THE MALE PATIENT

NORMAN TREVES, M.D., NEW YORK, N. Y.

(From the Breast Service, Memorial Hospital)

INFLAMMATORY carcinoma of the mammary gland is a most infrequent and interesting clinical variant. It comprises about 1.3 per cent of all breast cancers in women. Its infrequent incidence in women would seemingly indicate that it was of rarer occurrence in men. At the Breast Service of Memorial Hospital from 1925 to 1952, 131 cancers of the male breast have been observed. Among these, three instances of inflammatory carcinoma were in men, about 2 per cent. Thus, this type of cancer would appear to be twice as frequent in men as in women. In the three cases which have been observed, all were in men born in Russia of Jewish parents. We may only speculate as to the significance of this coincidence.

Reporting on the therapeutic effect of castration in cancer of the male breast in 1948, I included in that group of thirteen patients, two examples of inflammatory carcinoma. The primary purpose of that report was only to record the effects of orchiectomy and it was not to emphasize this rare and very malignant phase of mammary cancer. A remarkable third case of bilateral inflammatory carcinoma of the male breast appeared shortly after the publication of that communication.

A more extensive monograph on this phase of cancer in both sexes will appear at a later date.

In 1924, with Dr. Burton J. Lee, then Chief of the Breast Service at Memorial Hospital, I reported on twenty-eight cases of inflammatory carcinoma. This term we gave to this particular phase of mammary cancer after consulting with Dr. James Ewing, who supplied the histologic description of the tissues involved in our studies. A recent paper by Chris retained our nomenclature, since he felt that it was the best term to describe this condition and that "amongst the multitude of names so far suggested it still remains the most comprehensive and the most accurate description."

In our original communication we stated that carcinoma of the breast of the inflammatory type did not specifically appear during pregnancy or lactation as Volkmann, Billroth, and Schumann had recorded. Certainly its occurrence in the male patient negates any essential concomitance with gestation or the puerperium.

Previously this form of carcinoma of the male breast had been observed by Ritter, in 1936. Freeman and Lynch, in 1937, recorded a case which had been reported by Schreiner and Volvasek. The age incidence in men seems to be higher than in women, one patient being 66 years of age and the other

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two, 70 and 72 years of age, respectively. We reported in our initial series on women that 35.8 per cent were less than 39 years of age while the average age was 44.6 years. The oldest woman in the group was 62 years of age. The occurrence of this type of breast cancer seems confined to a later age in men. No explanation for this fact is offered; however, cancer of the breast in men usually occurs at a later age than in women.

We must consider the inflammatory aspect as a distinct clinical phase of mammary cancer and a most malignant and dramatically fatal form. As previously indicated, the cutaneous manifestations of the disease are histologically evidenced by invasion of the subepidermal lymphatics with cancer cells, the diffuse extension being the most distinctive microscopic pathologic feature. The disease may spread through the blood vessels as well. Ewing originally remarked that both lymphatics and venules were involved and that the tumor cells were generally mingled with red blood cells and some lymphocytes. The tumor cells showed marked degenerative changes including hydropic degeneration, swelling and hyperchromatism of nuclei, and isolated cell necrosis. Around all invaded vessels a rich exudation of small lymphocytes was present. The invasion of the subepidermal lymphatics and venules excited a lively venous congestion and a marked lymphocytic perilymphangitis and phlebitis.

Chris has added to the results of our studies his own observations and the reports of others. An unimportant controversy has occurred about the channels of spread in inflammatory carcinoma. The appearance of clumps of tumor cells lying within endothelial spaces in the subepithelial areas gave rise to a disagreement as to whether the spaces were vascular or lymphatic. Leitch, in 1909, described the microscopic spread of the invasive cells, calling attention to the subepidermal lymphatic permeation. The absence of erythrocytes in the tumor containing spaces led some investigators (Camiel and Bolker) to conclude that the permeated spaces were all lymphatic. Ewing was positive that blood vessel invasion occurred. Chris was unable to find blood vessel invasion within the skin but indicated that blood vessels in breast, liver, and lungs were involved by growth. The epidermis is uninvolved, as distinguished from its status in Paget's disease. The small subcutaneous blood vessels are variably but definitely dilated in the erythematous areas of skin, and in these areas there are perilymphatic collections of lymphocytes and plasma cells. Occasionally the subepidermal connective tissues are diffusely infiltrated by isolated cancer cells that have ruptured the walls of the lymph vessels.

The mechanism that produces the redness in the skin has not been satisfactorily explained. But dilation of the fine subpapillary blood vessels, whatever the cause, is responsible for the redness. The color may be the result of passive hyperemia but this alone is not the cause in every instance, since the skin is warm. This phenomenon must be due to an increased blood flow, the result of arteriole dilatation.

Chris stated: "The conclusion can be drawn that lymphatic channels appear to convey the tumor in the dermis and that the spread in the skin

through the blood vessels, although it has been shown to occur, is, relatively, an uncommon mode of spread in inflammatory carcinoma of the breast." This conclusion was based on these factors: (1) In some instances the diffuse infiltration of subepidermal connective tissue by isolated cancer cells had burst out of the small lymphatics; (2) there were perilymphatic collections of lymphocytes and plasma cells; (3) there was a variable but definite dilation of the small subcutaneous capillaries; (4) there was freedom of invasion of the epidermis; and (5) there was variable thinning and thickening of the epidermis. In the last instance he emphasized the acanthotic and hyperkeratotic proliferation.

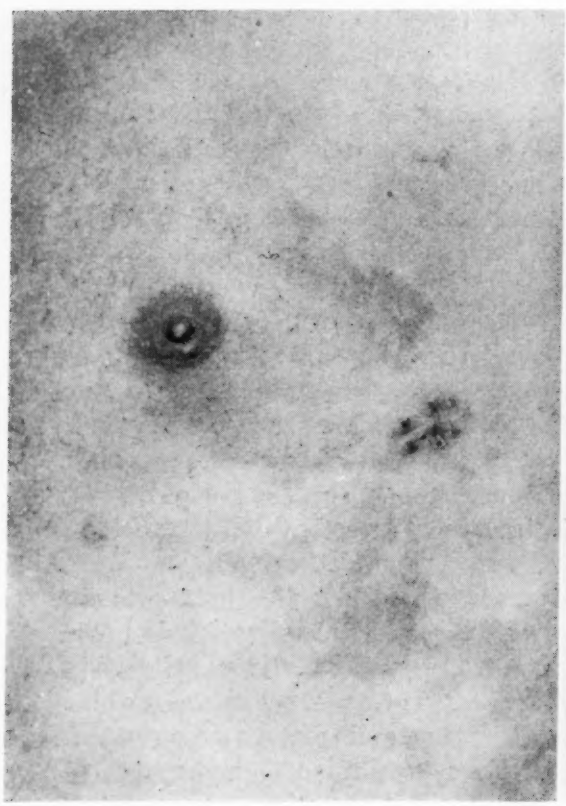

Fig. 1.

Fig. 2.

Fig. 1 (Case 1).—Photograph showing primary inoperable condition of the left breast on admission. The site of the cutaneous biopsy is lateral to the larger skin lesion.

Fig. 2 (Case 1).—Photograph showing failure of orchiectomy to affect the rapid growth of the lesion which involved the left hemithorax.

McMaster may have furnished a lead to the explanation of the inflammatory reaction in the skin, especially as it concerns the lymphatic participation in this unique cutaneous phenomenon. He stated: "The lymphatic capillaries possess walls that respond with remarkable rapidity to highly various stimuli and they are channels which take part actively in the process of fluid ex-

change. While they never become so permeable as to permit the immediate passages of particulate matter, nevertheless, at times, they cease to be walled off channels so far as physiological events are concerned.''

Fig. 3.

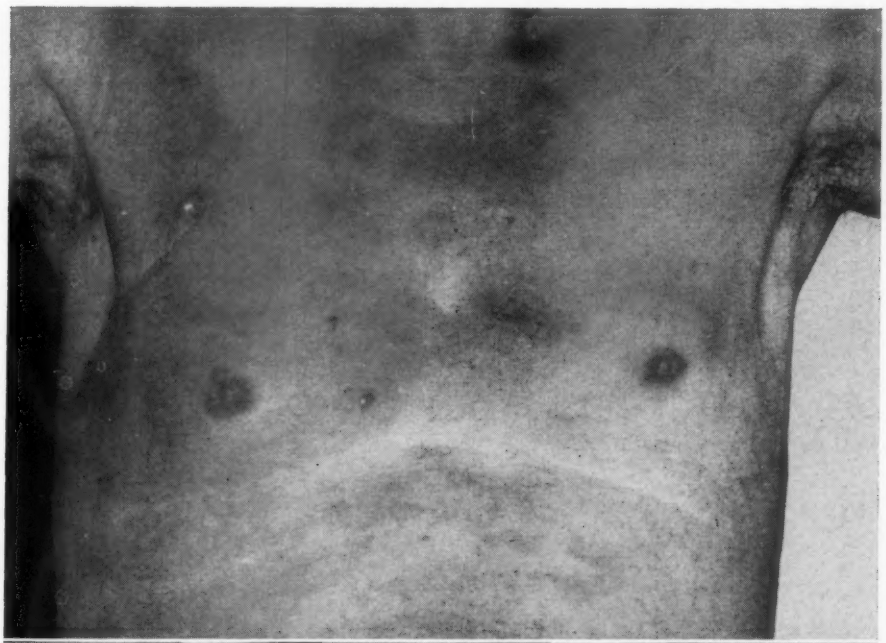

Fig. 4.

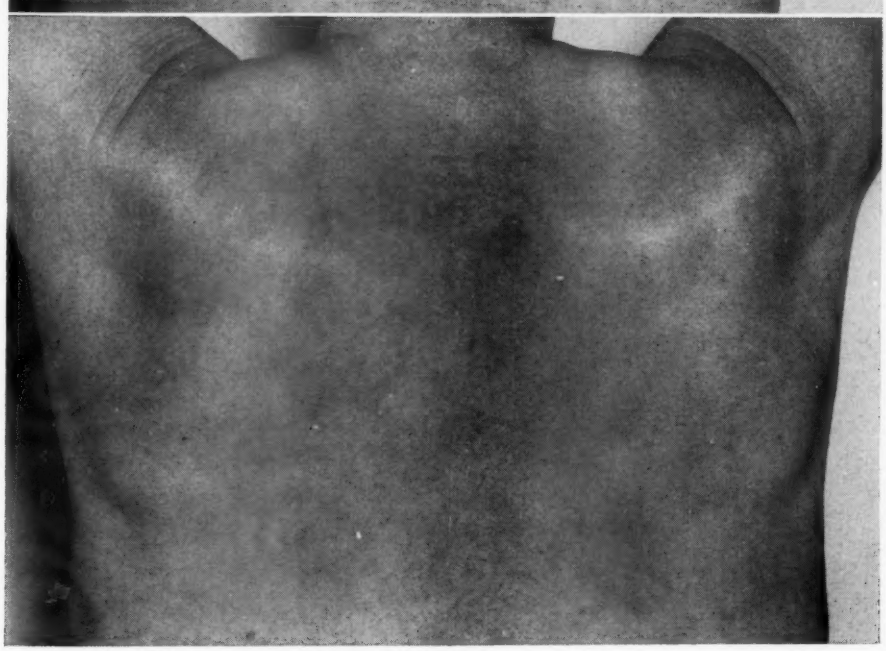

Fig. 3 (Case 2).—Photograph showing bilateral retraction by underlying mammary cancer. There is diffuse erythematous blush over entire anterior chest wall and abdomen. Scar of cutaneous biopsy of the left breast and vesicles in the skin of the right breast and anterior axilla may be seen.

Fig. 4 (Case 2).—Photograph showing extension of cutaneous involvement to skin over left scapula.

Willis satisfactorily explained the mechanism of the production of the cutaneous lesions in inflammatory carcinoma of the breast, although in his treatise he does not recognize this phase per se. He wrote: "Cancerous permeation and occlusion of the deep fascial plexuses, and cancerous replacement of superficial lymph glands, necessarily result in deviations of lymph flow in the subcutaneous and dermal lymphatic channels, often in a retrograded direction." One infers, therefore, that the rapidly growing primary tumor effectively blocks the afferent lymphatics and completely occupies the lymph nodes. As a result the only escape is by way of the periductal lymphatics and these extend to the base of the nipple and areola and finally to the subepidermal lymphatics.

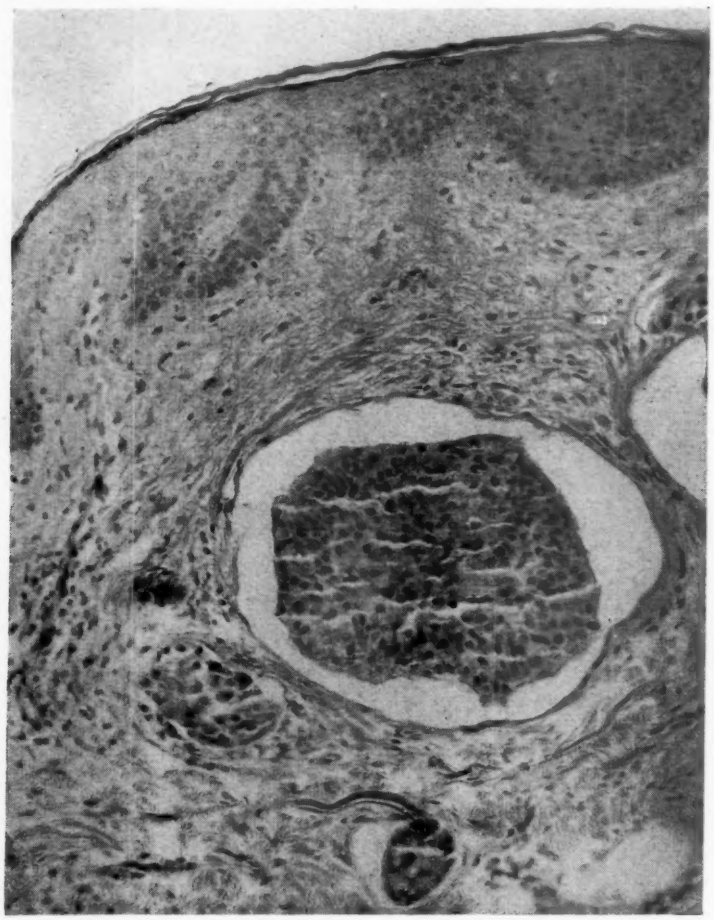

Fig. 5 (Case 2).—Photograph of biopsy of skin. Note thickened fibrotic epidermis with underlying edema of connective tissue. Blood vessel of subpapillary area is plugged with tumor thrombus. Lesser vessels are filled with tumor cells surrounded by infiltration of lymphocytes and plasma cells.

CASE REPORTS

The three histories of the cases of inflammatory carcinoma of the breast are presented. Two of these patients had primary inoperable lesions, one unilateral, the other bilateral. The third case recurred as inflammatory cancer after a radical mastectomy.

CASE 1.—B. G., aged 66 years, of Russian Jewish forebears, had one child. When admitted to Memorial Hospital on Aug. 25, 1947, he stated that a painless mass had appeared in the left axilla three months prior to the application for treatment. Two months later a herpetiform lesion appeared lateral to the left nipple; the lesion extended onto

Fig. 6.

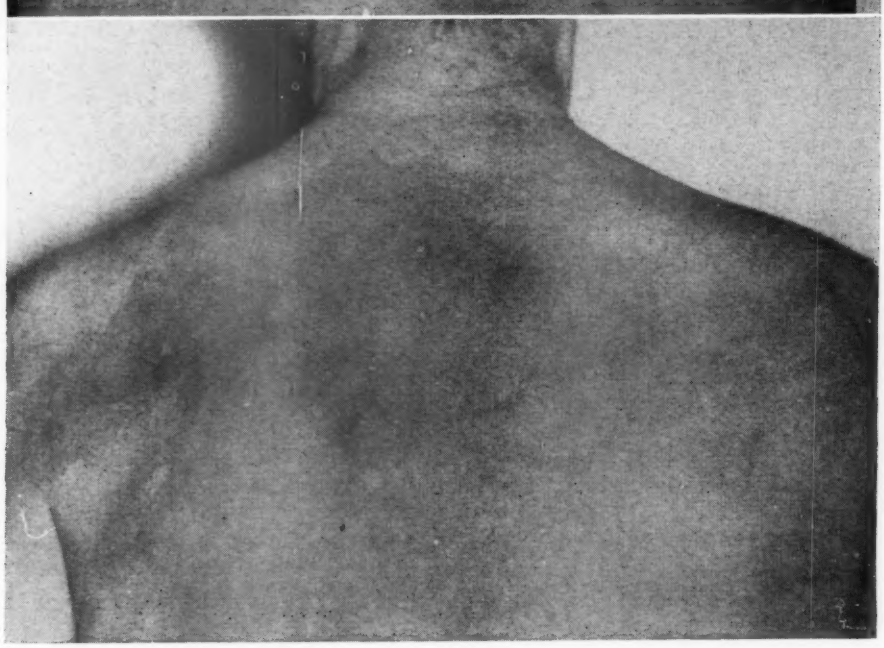

Fig. 7.

Fig. 6 (Case 2).—Photograph showing condition of breasts and skin two months after castration. The marked regression is not adequately conveyed by this illustration.

Fig. 7 (Case 2).—Photograph showing almost complete initial regression of the disease on the posterior chest wall. The slight erythema over the left scapula subsequently disappeared.

the left chest wall and almost to the vertebral column. An indefinite thickening could be palpated beneath the left breast. There were several enlarged nodes in the left axilla, the largest 2.5 by 1.5 cm. (Fig. 1). An incisional biopsy of the skin showed a structure resembling breast cancer. The aspiration biopsy of the node showed carcinoma. Roentgenograms of the chest showed no evidence of metastases. The blood chemistry was within normal limits.

Bilateral orchiectomy was performed on Oct. 1, 1947, under Pentothal Sodium anesthesia. The testes were moderately atrophic. Postoperative convalescence was uneventful.

Castration was without clinical effect. The tumor grew rapidly, involving the entire left hemithorax. Large vesicular blebs formed over the diffusely invaded skin. The lesions became quite painful (Fig. 2).

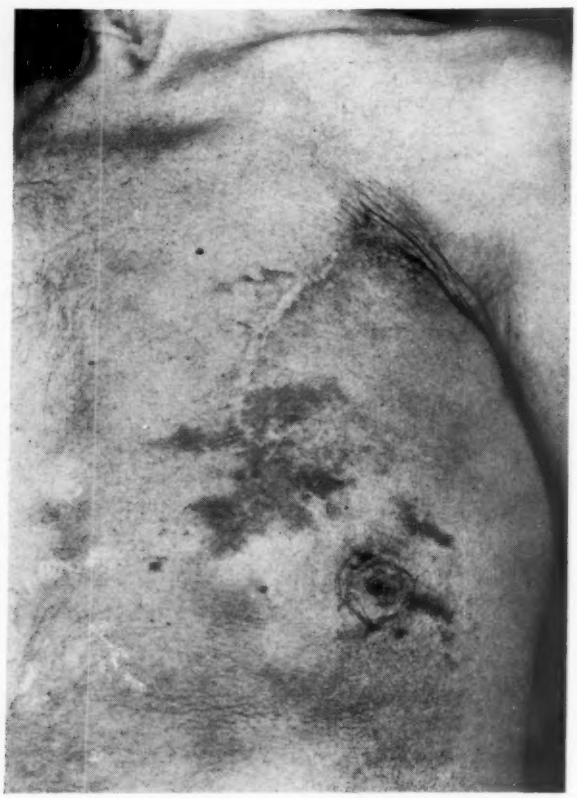

Fig. 8 (Case 3).—Photograph showing recurrent carcinoma of the left breast, inflammatory type.

We then employed irradiation of the pituitary gland giving a total of 2,100 r to each of three ports. This was without clinical effect. The study of the urinary ketosteroids continued. The patient lost ground rapidly. The lesion ulcerated, roentgen-ray therapy was without local effect, and "wasting" was quite rapid. The physical state approached that of Simmonds' cachexia and we entertained the idea that irradiation of the hypophysis might have been responsible.

The patient died Jan. 24, 1948, eight months after the onset of symptoms and almost four months after castration. This procedure in no way altered the clinical course. Postmortem examination was refused.

This was the first patient with primary inflammatory carcinoma of the male breast we had ever observed. Neither orchiectomy, irradiation of the

pituitary gland, nor, finally, local roentgen-ray therapy affected the constant progression of disease.

The second patient had an extensive bilateral mammary cancer in the inflammatory phase.

CASE 2.—L. E., white, a Russian Jew, 72 years of age, the father of three children, was first observed in the Memorial Hospital Breast Service on Oct. 10, 1949.

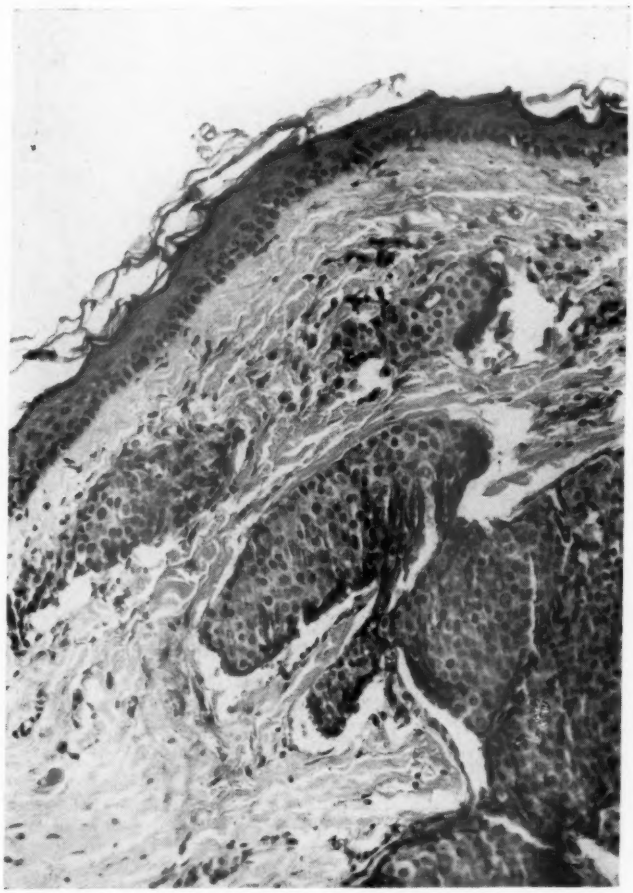

Fig. 9 (Case 3).—Photomicrograph of skin. The epidermis is normal. Subepidermal vessels are dilated with tumor cells which also lie loose in the stroma. A lively lymphocytic infiltration is present. A large plug of tumor cells is partially within and has ruptured through the vessel wall.

With the exception of several minor attacks of coronary disease seven years previously and a right femoral phlebitis that developed after an operation for a ruptured diverticulum of the large bowel fifteen years previously, he had been well. Increasing dyspnea and nocturia, with slight urinary obstruction, had been noted during recent years.

Through an interpreter he disclosed that the right breast became swollen and hard ten years prior to his first clinic visit. The hardness was diffuse, there being no localized tumor. Two years later, after he had been reassured that the condition was not serious, the opposite breast behaved in a similar fashion. The breasts had always been slightly enlarged and pendulous because of his obesity. Three months prior to admission (July, 1949) the right breast increased in hardness and there appeared a brilliant red blush in the mammary and pectoral areas, which spread rapidly over the skin of the left breast

and the chest wall laterally and posteriorly. The redness overlaid diffuse, brawny subcutaneous induration. The only tumor noted was a nodule in the skin of the left breast between the areola and sternum (Fig. 3). This area is represented by the biopsy scar. There were several vesicles in the skin of the right breast and anterior axilla. The right arm was swollen, probably because of metastatic axillary disease and involvement of the supraclavicular lymph nodes. (This had been treated as phlebitis at another hospital.)

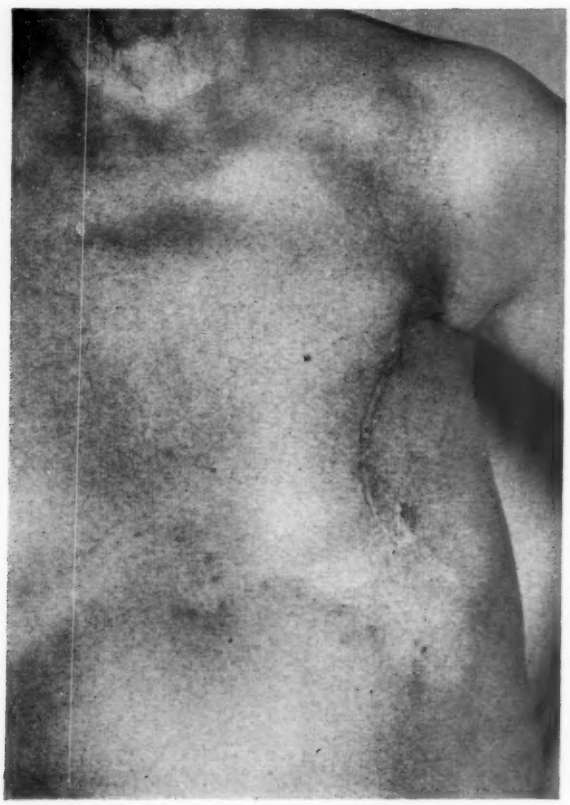

Fig. 10 (Case 3).—Photograph showing regression of the inflammatory manifestations after castration. Induration completely disappeared but very slight discoloration persisted. The crossed axillary metastasis showed total clinical disappearance.

Examination was entirely without positive findings except for the local condition. An erythematous induration of the skin with raised edge was observed over the chest anteriorly, laterally, and posteriorly extending over the left scapula where an elongated similarly indurated bright-red blotch was located (Fig. 4). The remaining cutaneous lesions extended girdle-fashion from the sixth to the tenth ribs from the midline posteriorly around the left side to the axilla and the entire breast area anteriorly. The right arm to the elbow was moderately swollen. Enlarged nodes could be palpated in the upper deep cervical area, the right submaxillary triangle, the right supraclavicular fossa, both axillary areas, and bilaterally in the inguinal region. The right supraclavicular and axillary nodes, especially on the right, were much larger and firmer than the rest.

A biopsy from the cutaneous nodule in the skin of the left breast on Oct. 15, 1949, was reported as mammary carcinoma permeating dermal lymphatics (Fig. 5).

Bilateral orchiectomy was performed Oct. 22, 1949, under Pentothal Sodium anesthesia. Convalescence was uneventful, the patient being discharged on the fifth postoperative day.

The pathologic examination showed atrophic and fibrotic testes with oligospermia.

On Nov. 3, 1949, remarkable regression in the subcutaneous induration and bleaching of the erythema was noted (Figs. 6 and 7). Two weeks later further diminution was observed with regression in the axillary nodes and disappearance of the supraclavicular nodes.

The swelling of the right arm had practically disappeared by Dec. 29, 1949, with further reduction in the size of the axillary nodes. The subcutaneous induration and discoloration had diminished to a remarkable degree. The patient felt particularly well.

When he was last observed on April 6, 1950, he was free of erythema and in good general condition. He died on May 14, 1950, quite suddenly, of coronary occlusion.

The third patient was observed in the recurrent phase of inflammatory cancer.

CASE 3.—J. G., aged 70 years, the father of five children, was of Russian Jewish ancestry. He was referred on March 17, 1947, for treatment of a recurrent breast cancer that had been operated upon Aug. 9, 1945. It had been diagnosed as anaplastic medullary carcinoma, metastatic to axillary lymph nodes. The referral was for immediate postoperative roentgen-ray therapy, but the patient failed to cooperate and received only inadequate dosage to three ports.

Examination revealed nothing of importance except in the left breast area, where there was the well-healed scar of a radical mastectomy. In the midportion on either side of the scar were two reddened patches of skin consisting of telangiectatic-appearing, dilated lymphatics with slightly raised borders. The area on the mesial side of the scar, about 3 by 4 cm., was better localized than the larger lateral area, which streaked off in the direction of the lateral chest wall and axilla. There was a metastatic node 2 cm. in diameter in the opposite axilla (Fig. 8).

The biopsy of a wedge of skin from the operative site showed mammary carcinoma invading the lymphatics (Fig. 9). Aspiration biopsy of the right axillary node was reported as carcinoma.

The patient was admitted for study prior to castration which was performed July 4, 1947, under Pentothal Sodium anesthesia. Convalescence was uneventful.

The pathologic examination showed atrophic testes.

The subsequent course showed that the cutaneous lesions had completely lost color (Fig. 10). The node in the right axilla became impalpable. Fifteen months after orchiectomy the patient had gained in weight and felt extremely well. However, in August, 1949, the patient developed a cough, which increased in severity. Two months later, a roentgenogram of the chest showed parenchymal metastatic lesions with evidence of lymphangitic spread. Death occurred about three months later, December, 1949, thirty months following castration, a procedure that obviously failed to influence dissemination of tumor.

CONCLUSIONS

Inflammatory carcinoma of the breast is an uncommon and rare phase of mammary cancer with an incidence of about 1 per cent of the malignant lesions of this gland, in women. Three cases of this form of breast tumor in 131 men have been observed in twenty-eight years' intensive observation of tumors of the mammary gland (2 per cent).

The histologic and clinical features of inflammatory carcinoma of the breast are identical in both sexes.

The clinical course is likewise identical, proving fatal in all three instances in men.

While the results in the two primary cases were not satisfactory, we still feel that patients with this type of the disease do better without surgery. The

first patient lived eight months, the disease unaffected by orchiectomy, by roentgen-ray therapy given locally and, later, administered to the pituitary gland. The second patient lived only six months but at the time of death, from coronary occlusion, the disease had shown a very favorable response to castration. The third patient whose only therapy was bilateral orchiectomy, seen in the recurrent phase, survived for the longest period.

The occurrence of three cases of inflammatory carcinoma of the male breast, all occurring in Russian Jews in the seventh and eighth decades of life, is of more than passing interest. Whether this incidence is significant as a racial tendency cannot be determined because of its extremely infrequent appearance.

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HEMORRHAGE FROM STRESS ULCER TREATED BY RESECTION

LIEUTENANT COLONEL ROBERT G. SALASIN, MEDICAL CORPS, UNITED STATES ARMY,* AND COLONEL WARNER F. BOWERS, MEDICAL CORPS, UNITED STATES ARMY,** FORT SAM HOUSTON, TEXAS

RENEWED attention recently has been given to the occurrence of acute ulcers of the upper gastrointestinal tract secondary to systemic stress, although this entity has been recognized for more than a century. This pathologic process was first described by Swan[1] in 1823 and by T. B. Curling[2] in 1842 when he observed and reported the development of acute erosions and ulcerations in the stomach and duodenum repeatedly in consequence of severe cutaneous burns. The term "Curling ulcer" has been used subsequently in description of such lesions. Harkins[3] has noted that the occurrence of gastrointestinal bleeding following burns is more common than coincidence would allow and, in reviewing ninety-four necropsy cases, he found that hemorrhage was twice as likely to be a fatal factor as perforation. Billroth[4] reported the first case of duodenal ulcer occurring postoperatively in 1867. More recently Penner and Bernheim[5] in 1939 reported four similar-type cases, all terminating fatally. Cushing[6] has reported acute gastric ulcer with perforation following brain operations. Ferguson and Wyman,[7] reviewing 157 cases of bleeding peptic ulcer, listed 28 cases as "acute syndrome," covering those in which an acute ulcer was seen, usually at necropsy, and those in which patients gave a history suggestive of ulcer of less than four weeks' duration, although no lesion could be demonstrated.

Ogilvie and associates[8] reported 358 cases of severe ulcer bleeding in which 19 were presumed acute ulcers. Woldman,[9] reviewing 943 necropsies, found 136 cases of acute ulcers and 108 cases of focal hemorrhages, which he thought to be the initial lesion of an acute ulcer in some instances. Of the 136, 36 were in postoperative patients, the operation or emotional tension attached being considered the stimulating stress factor.

Etiology.—Selye[10] has reported the production of acute ulcerations of the upper gastrointestinal tract during the alarm reaction following systemic stress, and has further shown that various stresses, such as trauma, surgery, burns, infections, fatigue, and emotional tension, may produce such alarm reactions. In addition, these lesions were more readily produced experimentally in animals following adrenalectomy. Similarly, Woldman[9] noted that the incidence of ulcers and mucosal hemorrhages was highest in terminal conditions, which were more likely to be associated with shock, and that the greater the adrenal damage as shown by microscopy the greater the incidence of ulceration of the gastrointestinal tract, supporting the prevalent contention

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*Assistant Chief, Surgical Service, Brooke Army Hospital.
**Chief, Surgical Service, Brooke Army Hospital.

that the adrenal gland is a stress defense organ. The literature contains ever-increasing numbers of case reports of gastric or duodenal ulcers being produced during prolonged ACTH therapy, a situation simulating chronic stress, since it elicits many of the same responses as those of sustained alarm. The effect is usually due to the secondary outpouring of the adrenal cortical steroids rather than to the primary action of ACTH itself, as may be well demonstrated in patients with adrenal insufficiency. Although the gastric response to stress is undoubtedly mediated in part, at least through the vagus nerve, Gray[11] has presented evidence strongly suggesting that an additional hormone mechanism is involved which is ultimately associated with the general adaptation syndrome as described by Selye.[10] The suggested chain of stimulus has been from hypothalamus to pituitary gland to adrenal cortex to the gastric glands.

From a clinical viewpoint, it is difficult to obtain facts supporting these acute ulcers since they usually heal very rapidly once the stress factors have been removed, the majority healing without a trace of evidence of preexistence.

Then again, the stress factor may be a terminal one, and the symptoms of ulcerations and erosions may not be noted in the dearth of other terminal symptoms, or the ulcerations may be considered as being due to post-mortem changes when the patient eventually comes to autopsy. Acute ulcerations are said to be difficult to demonstrate radiographically.

Harkins[3] noted that up to 1942 no acute ulcer following burns had been treated surgically. Braithwaite,[12] in 1948, reported subtotal gastrectomy for hemorrhage from a chronic peptic ulcer following a cutaneous burn, with resultant cure. Wangensteen and co-workers[13] reported on ten patients who developed severe peptic-ulcer disease for the first time as the result of the stress of a surgical operation, or the administration of ACTH or cortisone, with five fatalities. Of the five patients who survived, three recovered with nonoperative therapy in spite of severe gastroduodenal hemorrhages. Two others required subsequent subtotal gastrectomy.

The foregoing facts have been discussed as an introduction to a case report in which an acute gastric ulcer with massive hemorrhage developed in an elderly postoperative patient, was demonstrated by barium x-ray studies, and was successfully treated by surgical intervention.

CASE REPORT

J. J. M., a 73-year-old white man, a retired master sergeant, was admitted to Brooke Army Hospital on July 11, 1952, complaining of fever, low back pain, constipation, ten-pound weight loss, dysuria, and cloudy urine. Diagnostic work-up revealed a large tumor of the left kidney; infiltration in the left lung field was considered to be the residual of old infection. On Sept. 2, 1952, a left nephrectomy was performed with a postoperative pathologic diagnosis of Grawitz' tumor being made. Postoperatively the patient apparently did well until Sept. 11, when he had an episode of auricular fibrillation which was treated with Cedilanid and digitalis and his rhythm converted to normal. On Sept. 12, 1952, the patient was noted to have a coffee-ground emesis measuring approximately 200 cubic centimeters. Early in the morning of Sept. 13, 1952, the patient developed a marked

drop in blood pressure, an increase in pulse, and marked hematemesis. The patient was treated with blood replacement, 3,500 c.c. being given in twenty-four hours, and he apparently responded well, the blood pressure returning to 160/70 and the pulse to 98. At this time the patient was seen by both the gastroenterology service and the surgical service and a gastrointestinal x-ray series was then performed revealing at fluoroscopy and on films a constant collection of barium in the antral portion of the stomach which was interpreted as a presumptive gastric ulcer. On Sept. 14, 1952, the patient again had a sudden drop in blood pressure, 74/40, an increase in pulse, 128, and a marked increase in the amount of blood removed by Levin tube and suction. Five hundred c.c. of whole blood was started, but it was felt that the patient had experienced a second massive hemorrhage from the ulcer and was losing ground on conservative management. The patient was then prepared for operation and a subtotal gastric resection was performed with a retrocolic Hofmeister gastrojejunostomy. The patient withstood the operative procedure well. The Levin tube was removed on the third postoperative day and gradual feeding was started thereafter. On the fourth postoperative day the patient developed superficial thrombophlebitis secondary to continuous intravenous therapy, which responded well to conservative management and was cured by the eighth postoperative day. The most trouble encountered with the patient postoperatively was his poor interest in eating, although the family substantiated this condition prior to his entry into the hospital.

Pathologic Diagnosis.—The diagnosis was acute gastric ulcer.

Gross.—On examination of the mucosa there was an ulceration of the mucosa 1 cm. in diameter which was situated 4 cm. from the cardiac end of the stomach near the lesser curvature proper. Perpendicular to the line of tissue there was a 0.2 cm. in diameter circular structure with a lumen of 0.1 cm. which represented a large vessel in the middle of the ulcer. The base of the ulcer was grayish colored except in the central portion around the blood vessel where it was reddish brown. On close examination the ruga and markings of the remainder of the specimen appeared to be normal. On cross section through the ulcer, three small blood vessels 0.1 cm. in diameter were seen deep in the tissue, of which the lumina remained open.

Microscopic.—One slide presented a section of gastric mucosa which showed the presence of a marked ulceration in the mucosal surface with a marked inflammatory infiltration composed mainly of polymorphonuclear leukocytes. The gastric glands adjoining the edges of this ulcer were normal in appearance and presented the usual tublar-type mucous glands.

Discussion.—The management of hemorrhage from peptic ulcer has caused controversy as to whether conservative medical measures or surgical intervention is most successful. Statistics support both methods of treatment. Surgical intervention, usually subtotal gastrectomy, has carried the following mortality rates in various reported series: (1) Gordon-Taylor,[14] 18.3 per cent in 71 cases; (2) Dunphy,[15] 10 per cent in 11 cases; (3) Stewart,[16] 10.7 per cent in 65 cases; (4) Allen,[17] 14.6 per cent in 144 cases; (5) Finsterer,[18] 5.9 per cent in 51 cases; (6) Brown,[19] 11.1 per cent in 36 cases; (7) Heuer,[20] 29 per cent in 31 cases; and (8) Connolly,[21] 13 per cent in 33 cases. Higher mortality rates were noted by (1) Crohn,[22] 71.4 per cent in 7 cases; (2) Ross,[23] 60.4 per cent in 43 cases; and (3) Aitken,[24] 33.3 per cent in 21 cases. Finsterer,[18] Heuer,[20] Chinn,[25] and others have noted that surgical mortality is lowered if early operation is practiced; that is, in Heuer's 31 cases, the mortality rate was only 10 per cent for patients undergoing early operation and 70 per cent for those operated on late. Those series with higher surgical mortality rates usually are made up of many patients who were treated conservatively for several days and when these measures failed were then given surgical treatment.

Mortality under medical management is likewise impressive in the following series: (1) Stewart,[16] 21 per cent in 42 cases; (2) Connolly,[21] 4 per cent in 173 cases; (3) Lipp,[26] 14.8 per cent in 274 cases; and (4) Higgins,[27] 2.1 per cent in 46 cases.

Extremes of treatment, whether on the medical or surgical side, are probably to be condemned. Observation of the bleeding-ulcer patient by both medical and surgical services is preferable, with management started conservatively with blood replacement; the point being kept in mind that, should the patient fail to show appreciable improvement within the first twenty-four hours, he should be considered a candidate for immediate operation. Many other factors are to be considered in the specific cases, such as age of the patient (the mortality rate being higher in the older groups), the location of the ulcer (mortality being higher from gastric ulcers than from duodenal ulcers[28]), and severity of hemorrhage (probably most important in making the decision to treat by surgery).

Surgical Management.—The operative procedure to be undertaken will be determined by the condition of the patient and the location of the ulcer. The operation of choice is subtotal resection with emphasis on two principles: (1) ligation of the blood supply to the ulcer as rapidly as possible, and (2) high enough resection to remove the ulcer and 75 per cent of the acid-producing portion of the stomach. Ogilvie[8] has reported a case in which subtotal resection was performed for hemorrhage with death occurring two days later due to hemorrhage from multiple acute erosions throughout the mucosa of the gastric remnant. Control of bleeding by ligation of the artery in the ulcer bed should be reserved for that small percentage of patients whose condition is precarious, inasmuch as recurrence of bleeding is common when such procedure is undertaken.

CONCLUSIONS

Acute gastric or duodenal ulcer should be strongly considered in sudden gastrointestinal hemorrhage following operation on systems other than the upper gastrointestinal tract, even in absence of previous "ulcer" history. Roentgenography with barium swallow will be helpful in establishing diagnosis in the majority of cases. Hemorrhage, if severe, is best managed by replacement of blood and early subtotal gastrectomy, with emphasis being placed on adequate resection of ulcerated mucosa.

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GASTROINTESTINAL ULCERATIONS COMPLICATING BURNS

A Report of Five Cases and a Review of Seventeen Cases Reported From 1942 to 1952

Captain Arthur E. Weigel, Medical Corps, United States Air Force, Major Curtis P. Artz, Medical Corps, United States Army, Captain Eric Reiss, Medical Corps, United States Army, Captain John H. Davis, Medical Corps, Army of the United States, and Colonel William H. Amspacher, Medical Corps, United States Army
Fort Sam Houston, Texas

(From the Surgical Research Unit, Brooke Army Medical Center)

SPORADIC reports of gastrointestinal ulcerations that occur after burns have appeared in the literature since Curling called attention to this problem in 1842. Harkins reviewed the literature up to 1938[6] and found 107 cases of gastrointestinal ulceration associated with burns, including 94 cases with autopsy and 13 with recovery. In 1942,[7] Harkins added ten cases to his original series. A review of the literature from 1942 to 1952 has revealed reports of seventeen additional cases.

Since December, 1949, 600 burned patients have been hospitalized at the Burn Study Section of the Surgical Research Unit, Brooke Army Medical Center.[1] Of the 20 patients who died, 5 had proved gastrointestinal ulcerations. This report includes these five cases and a summary of pertinent clinical and pathologic observations derived from a review of the seventeen cases reported in the literature since 1942.

CASE REPORTS

Case 1 (Brooke Army Hospital No. 2785026).—A white man (D. D. W.), a pilot 23 years of age, was rescued two hours after his plane exploded and burned as the result of a crash landing. He received full-thickness burns of 25 per cent of the body surface and partial-thickness burns of 20 per cent. The areas involved were the face, scalp, neck, posterior aspect of the trunk, and the upper and lower extremities. Other injuries or organic disease was not evident. There was no history of gastrointestinal symptoms before injury.

Shock was adequately controlled by the use of whole blood and 0.9 per cent saline solution, given intravenously, and a salt-soda solution, given orally. Local care consisted of a minimum of débridement and of occlusive, absorptive dressings. During the first three postburn days, the patient received a total of 425 mg. of cortisone intramuscularly. Procaine penicillin, 300,000 U., was administered every twelve hours throughout the patient's hospital course. After the third postburn day, the patient was given a high-caloric, high-protein diet with vitamin supplements.

The patient's temperature was 106° F. on the third postburn day and 105° F. on the sixth postburn day. In the interim, temperatures of 100° to 102° F. were recorded. On admission to the local station hospital, the red blood count was 7,360,000 and the hemoglobin 24.8 Gm.; on the fourth postburn day, the red blood count was 4,620,000, the hemoglobin 13.5 Gm., and the hematocrit 50.

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The patient was transferred by air evacuation from the local station hospital to Brooke Army Medical Center on the ninth postburn day. The patient's general condition was satisfactory, except for clinical evidence of a water deficit of considerable magnitude. The hemoglobin was 16.5 Gm., hematocrit 47, white blood count 8,400, serum sodium 142 meq. per liter, serum potassium 3.6 meq. per liter, serum chlorides 114 meq. per liter, serum bicarbonate 28 meq. per liter, total proteins 4.57 Gm., albumin 2.19 Gm., and globulin 2.38 grams. Except for an increase in the serum sodium to 155 meq. per liter and a decrease in the serum potassium to 2.8 meq. per liter, the electrolyte concentrations in the plasma remained essentially unchanged throughout the remainder of the patient's hospital course.

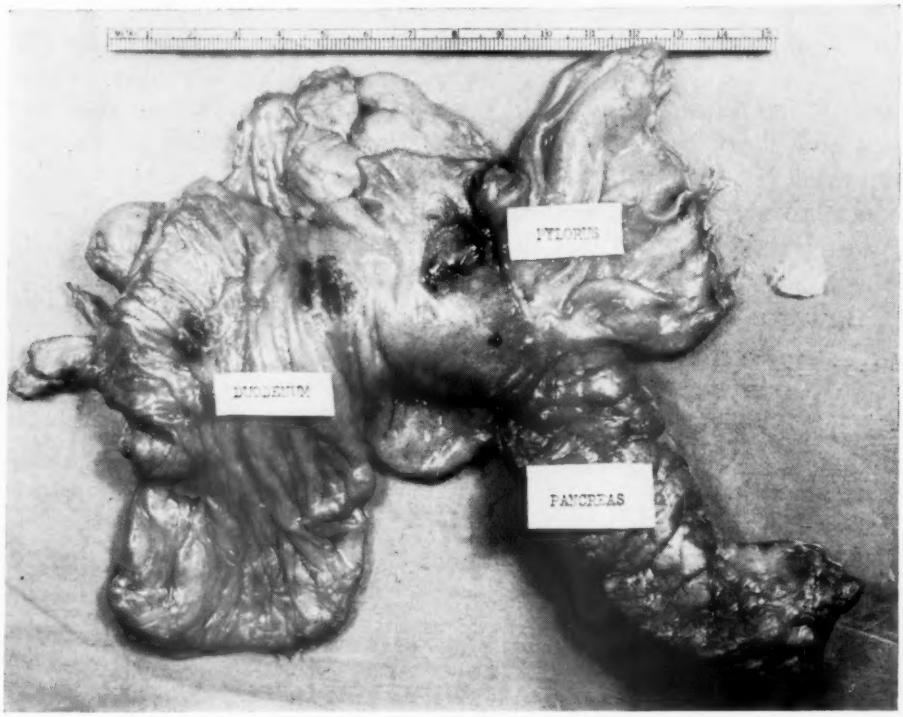

Fig. 1.—Autopsy specimen from patient in Case 1. Three ulcers are present in the posterior aspect of the duodenum. The two small ulcers are rather shallow, while the large ulcer near the pylorus is quite deep. Massive hemorrhage with exsanguination occurred from the superior pancreatoduodenal artery, located in the base of the large ulcer.

On the tenth postburn day, a tracheotomy was performed to facilitate the administration of general anesthesia, and the dressings were changed. On the evening of that day, the patient passed two liquid, tarry stools, the blood pressure decreased to 92/54, and the hematocrit decreased to 32. After the administration of 1,500 c.c. of blood and 1,500 c.c. of saline solution, the blood pressure returned to normal. The patient was given atropine, and a Sippy diet was prescribed. On the twelfth postburn day, bleeding recurred and approximately 2,000 c.c. and 800 c.c. of blood were lost by emesis and by defecation, respectively. Gentle intermittent gastric suction was instituted, and the blood loss was again successfully replaced by the administration of 4,400 c.c. of blood and 2,000 c.c. of normal saline solution. On the morning of the thirteenth postburn day, signs of profound shock and cyanosis suddenly developed and, despite a massive intra-arterial transfusion of blood, the patient died.

Autopsy Findings.—There were approximately 1,000 c.c. of partially clotted blood in the stomach, and an equal amount was in the intestinal tract. Three acute ulcers were evident in the duodenum (Fig. 1). The largest ulcer, situated on the posterior aspect of

the first part of the duodenum, measured 1.2 cm. in diameter. The base was smooth, gray, and glistening, and the borders were not indurated. A perforated artery (superior pancreaticoduodenal) was seen in the ulcer crater. Except for the large ulcer, which had eroded through the muscular layer to the underlying artery, only denuded mucosa was seen on microscopic examination of the other ulcers. The cellular response in the superficial areas was slight; in the deep layers it was marked. Most of the cells were eosinophils and lymphocytes with a few monocytes and polymorphonuclear leukocytes. A section of the stomach showed a small superficial ulceration of the mucosa with eosinophilic cellular infiltration.

Discussion.—The first sign of gastrointestinal ulceration was rectal bleeding, which occurred on the tenth postburn day. Conservative therapy was instituted and the hemorrhage ceased, but two days later the patient experienced a second massive hemorrhage. The blood was again satisfactorily replaced and the patient's condition improved until the thirteenth postburn day, at which time a third massive hemorrhage occurred and the patient died from exsanguination. Autopsy revealed four acute ulcers of the intestinal tract, the largest of which was in the posterior aspect of the duodenum and had eroded into the pancreaticoduodenal artery.

In retrospect, it appears that surgical intervention to control the hemorrhage should have been carried out when the second hemorrhage occurred. Because of the lack of chronic inflammatory reaction and of scarring, subtotal gastrectomy would have been technically less difficult than in chronic duodenal ulcer. This patient's life might have been saved had the same principles of therapy for the treatment of hemorrhage from this ulcer been used as are accepted in the treatment of bleeding from chronic duodenal ulcerations, that is, subtotal gastrectomy if a second massive hemorrhage occurs during conservative management.

CASE 2 (Brooke Army Hospital No. 2342053).—A white man (J. D. H.), 20 years of age, received full-thickness burns of 36 per cent of the body surface and partial-thickness burns of 9 per cent in a fire caused by the careless use of gasoline. The burned areas were the forearms, the entire lower extremities, the buttocks, and the left anterior portion of the trunk. Other injuries or organic disease was not demonstrated. There was no history of gastrointestinal symptoms before injury.

Shock was adequately controlled, and occlusive, absorptive dressings were applied. Cortisone and ACTH were not given. The patient received 300,000 U. of procaine penicillin every twelve hours for the first ten days. The patient was transferred to the Brooke Army Medical Center on the twelfth postburn day. On the twenty-second postburn day, split-thickness grafts were applied to the upper and lower extremities. On the thirty-third postburn day, additional grafts were placed on the lower extremities. At the first dressing after the last grafting, massive surface infection with complete loss of the grafts was noted. Cultures of the wound revealed beta hemolytic Streptococcus, hemolytic *Staphylococcus aureus,* and *Pseudomonas aeruginosa.* On the thirty-eighth postburn day, a daily temperature increase to from 102° F. to 104° F. was recorded, and the patient became disoriented. Intermittent fever and disorientation persisted until the patient died. The clinical diagnosis was septicemia, but blood cultures taken on six occasions failed to prove this diagnosis, possibly because of the massive doses of various antibiotics that were given on an empirical basis. On the forty-eighth postburn day, the patient suddenly became nauseated, vomited 400 c.c. of bright red blood, and passed several tarry stools. He was given 3,500 c.c. of whole blood and atropine, and a Sippy diet was prescribed. Further signs of hemorrhage were not noted. On the fifty-fifth postburn day, the abdomen

became distended, bowel sounds were faint, and tenderness was elicited in the upper portion of the abdomen. The next day, the distention was markedly increased, and the presence of a large amount of free air was revealed by roentgenography. Gastric suction and fluid and electrolyte replacement therapy were instituted, and terramycin was given intravenously. Localized tenderness was evident in the upper portion of the abdomen on the fifty-ninth postburn day, and incision and drainage of an abdominal abscess were carried out. Drains were inserted into the abscessed area, but the patient's condition did not improve. He died on the sixty-fifth postburn day.

Autopsy Findings.—Two perforated ulcers on the anterior surface of the stomach, extensive peritonitis, and a large pelvic abscess were noted. In addition, a large amount of blood was found in the lumen of the small intestine and in the peritoneal cavity. A section of the stomach wall in the vicinity of the ulcers showed infiltration by lymphocytes and polymorphonuclear leukocytes and marked thickening as a result of extensive fibrosis. There was moderate congestion and early central necrosis of the liver. A mild pyelitis was present.

Discussion.—The patient's course appeared to be satisfactory until the thirty-third postburn day, when a massive infection was noted over the extensive granulating surfaces. Antibiotics and frequent dressing changes did not alter the patient's condition and, on the forty-eighth postburn day, bleeding from the gastrointestinal tract occurred. Seven days later the ulcerative lesions in the stomach perforated and the patient died because of overwhelming peritonitis. It appeared that the infection in the large burn wounds was extremely debilitating and that the ulcerative lesions in the stomach were directly responsible for the patient's death.

CASE 3 (Brooke Army Hospital No. 2804045).—A white man (G. D. B.), 30 years of age, was burned in a gasoline fire that occurred after a B-29 aircraft in which he was flying crashed. He received full-thickness burns of 55 per cent of the body surface. The entire face, neck, upper extremities, groins, buttocks, thighs, and part of both legs were involved. There was no history of gastrointestinal symptoms before injury.

The patient was given whole blood and saline solution, but the electrolyte therapy was inadequate. The burns were treated by the exposure method. The patient was transferred to the Brooke Army Medical Center by air evacuation on the tenth postburn day. On examination, there was clinical evidence of a profound deficit of water and electrolytes. The serum sodium was 170 meq. per liter, serum potassium 4.4 meq. per liter, serum chlorides 121 meq. per liter, and the serum bicarbonate 28 meq. per liter. The red blood count was 5,770,000, hemoglobin 17 Gm., and hematocrit 56. After appropriate fluid therapy, the serum sodium decreased to 153 meq. per liter, the red blood count to 5,350,000, the hemoglobin to 13 Gm., and the hematocrit to 50. However, the patient's condition failed to improve; the temperature gradually increased to 105.6° and the pulse rate to 146. The patient became progressively more delirious. He finally became comatose and expired on the thirteenth postburn day.

Autopsy Findings.—There was a moderate amount of pulmonary edema with hemorrhage and congestion of the lower lobes of both lungs. One small pulmonary infarct was seen in the right lung. There were a few scattered microscopic hemorrhages in the brain at the base of the third ventricle. Examination of the duodenum revealed several small ulcers. A large ulcer, which mesaured 1.5 by 0.5 cm., was situated on the posterior aspect of the first part of the duodenum overlying the pancreaticoduodenal artery. This ulcer was shallow and its borders were not indurated. The other ulcers were superficial and did not measure more than 3 mm. in diameter. Microscopic examination of the largest ulcer revealed an extension of the erosion through the mucosa and into the muscular wall. The cellular response to ulceration was slight, and only a few scattered monocytes were seen.

Discussion.—The pathologic process that caused this patient's death could not be accurately determined. From the clinical data, it was believed that severe intracellular dehydration was the cause of death. The large, acute ulcer on the posterior aspect of the duodenum was directly over the pancreaticoduodenal artery. Although this ulcer did not produce any signs or symptoms, it could have caused hemorrhage if the patient had lived longer.

CASE 4 (Brooke Army Hospital No. 2838042).—A Negro man (C. W.), 65 years of age, was burned when a mixture of paint thinner exploded. He received full-thickness burns of 25 per cent of the body surface and partial-thickness burns of 15 per cent. The burns involved the anterior and posterior surfaces of the chest, back, right thigh, entire left lower extremity, left upper extremity, and right forearm. There was no history of gastrointestinal symptoms before injury.

The patient was admitted immediately to Brooke Army Medical Center. During the first forty-eight hours, he was given dextran, lactated Ringer's solution, and 5 per cent glucose in water, intravenously. On the basis of the clinical response to therapy, urinary output, and repeated plasma volume determinations by the T 1824 dye technique, this therapy appeared to be adequate. The burned areas were cleansed, all devitalized epidermis was removed, and occlusive, absorptive dressings were applied. Except for a slight hemoconcentration on the first postburn day (hematocrit 56, red blood count 6,350,000, and hemoglobin 14 Gm.) and an increase in the nonprotein nitrogen to 63 mg. per 100 c.c. of plasma on the second day, significant changes were not observed in the laboratory studies. The patient received 2,000,000 U. of crystalline penicillin on admission and 600,000 U. of procaine penicillin every twelve hours thereafter.

Abdominal distention was noted on the first postburn day and persisted until death. On the fourth postburn day, the patient's temperature increased to 102.6° F., he became disoriented, and the blood pressure decreased to 60/40. Signs of left ventricular failure developed, but the patient's condition improved after rapid digitalization. Hypotension persisted, however, and the blood pressure stabilized at 70/40; the infusion of blood and vasopressor substances only transiently increased the blood pressure. Gastric dilatation developed, and intermittent suction therapy, through an intragastric tube, was instituted. On the basis of a very high urinary-sodium excretion, low potassium excretion, and hypotension, a diagnosis of adrenocortical insufficiency was made on the fifth day. Aqueous adrenocortical extract was given intravenously, and cortisone was given orally and intramuscularly. The patient became anuric, his temperature increased to 102° F., and he became progressively weaker. He died on the sixth postburn day. A blood culture was obtained on the fourth postburn day, but its results were not known until after the patient's death; it revealed a beta hemolytic Streptococcus, Aerobacter, Klebsiella, and paracolon bacillus.

Autopsy Findings.—There was an acute endocarditis of the aortic valve. Both lungs showed focal hemorrhage and congestion. There was a moderately severe pyelonephritis in both kidneys. A small area of infarction and acute focal embolic glomerulonephritis was seen in the right kidney. A section of the stomach showed ulceration of the mucosa. The margins of the ulcer were elevated, and there was very little infiltration by inflammatory cells. One large ulcer, 1.5 by 1.0 cm., was present on the posterior surface of the first portion of the duodenum. Eosinophilic staining fibrinous material was present at the margins of the ulcer. There was no infiltration by inflammatory cells, and the adrenals were essentially normal.

Discussion.—The patient had a very extensive burn complicated by an acute bacterial endocarditis. Although he expired as early as the sixth postburn day, acute ulceration of the stomach and duodenum were noted at autopsy.

CASE 5 (Brooke Army Hospital No. 2124055).—A white man (T. R. B.), 28 years of age, was admitted to Brooke Army Hospital because of burns that he received when a butane gas heater exploded. Full-thickness burns extended over 70 per cent of the body surface and partial-thickness burns over 15 per cent. The burns involved almost all areas of the body except the scalp, feet, and ankles. Other injuries were not evident. There was no history of gastrointestinal symptoms before injury.

Immediate fluid replacement therapy appeared to be adequate. Large dressings were applied to the posterior surfaces of the body; the anterior surfaces were treated by the exposure method. The patient received 600,000 U. of penicillin daily and 40 mg. of ACTH intramuscularly every twelve hours. There was no evidence of infection in the burn wound, and gastrointestinal signs and symptoms were absent. For unknown reasons, the patient became comatose and anuric on the fourth postburn day, and he died.

Autopsy Findings.—There was severe congestion in both lungs and a moderate amount of pulmonary edema, bilaterally. Early focal abscesses in the right lung and focal hemorrhages in the pleura of both lungs were evident. The spleen and liver were acutely congested. Both kidneys showed small areas of the focal hemorrhage. Two centimeters below the pylorus on the posterior aspect of the duodenum was a hemorrhagic, superficial ulceration of the duodenal mucosa, which measured 0.6 cm. in diameter. There were several small hemorrhagic ulcerations in the third portion of the duodenum and the first portion of the jejunum and a few mucosal hemorrhages in the ileum.

Discussion.—The patient had burns of 85 per cent of the body surface, but the immediate fluid replacement therapy appeared to be adequate. ACTH was given intramuscularly on an experimental basis. The patient expired on the fourth postburn day. The cause of death was obscure; at autopsy, the anatomic findings were not sufficient to explain the mechanism of death. Several small ulcerations were seen in the duodenum and ileum, but these lesions did not cause any symptoms.

OBSERVATIONS ON THE COLLECTED SERIES (TWENTY-TWO CASES)

The pertinent facts of the five cases presented and the seventeen cases reported in the literature from 1942 to 1952 are summarized in Table I. Cases 1 through 12 include patients who had deep burns of a large percentage of the body surface. All were young or middle-aged, and none survived. In Cases 13 and 14, the patients had very superficial burns over a large percentage of the body surface; neither patient survived. In Cases 15 through 20, the patients were very young or very old and had small or moderate burns; none survived. In Case 21, a duodenal ulcer eroded into the gastrointestinal artery of a man, 52 years of age, who had a very small burn. An emergency subtotal gastrectomy was performed on the fourteenth postburn day, and the patient's postoperative course was uneventful. In Case 22, the history of a man 36 years of age who had a deep burn of 33 per cent of the body surface, severe melena developed on the fifteenth postburn day. A roentgenogram of the upper gastrointestinal tract revealed a duodenal ulcer. He was placed on a Sippy diet, and conservative treatment with the use of atropine and whole blood was carried out.

Prodromal symptoms were not evident in most cases in which hemorrhage and perforation occurred. In Cases 3 through 7, the patients died of causes other than gastrointestinal ulceration, and in these patients signs or symptoms of gastrointestinal disease were completely absent.

TABLE I. CORRELATION OF EXTENT OF BURN WITH ULCERATION (22 CASES, 1942 TO 1952)

CASE	REFERENCE	AGE (YR.)	SURFACE AREA BURNED				LOCATION OF ULCERS	CAUSE OF DEATH
			FIRST DEGREE (PER CENT)	SECOND DEGREE (PER CENT)	THIRD DEGREE (PER CENT)	TOTAL (PER CENT)		
1	Weigel et al.	23	0	20	25	45	Duodenum, multiple, posterior	Hemorrhage
2	Weigel et al.	20	0	9	36	45	Stomach and duodenum, multiple	Perforation (stomach) with peritonitis
3	Weigel et al.	30	0	10	55	65	Duodenum, multiple	Fluid and electrolyte imbalance
4	Weigel et al.	65	0	15	25	40	Duodenum and stomach, multiple	Bacterial endocarditis
5	Weigel et al.	28	0	25	60	85	Duodenum, multiple	Fluid and electrolyte imbalance
6	Prosinger[17]	40	0	—	44 —	44	Terminal ileum, multiple	Fulminating infection
7	Prosinger[17]	33	0	7	40	47	Pharynx and lower esophagus, multiple	Fulminating infection
8	Verdan[22]	40	0	—	60 —	60	Stomach lesser curvature	Perforation with peritonitis
9	Whigham[23]	26	0	—	50 —	50	Duodenum, posterior	Hemorrhage
10	Braithwaite and Beales[2]	26	0	25	40	65	Duodenum, posterior	Hemorrhage
11	Mynhardt[15]	34	0	—	64 —	64	Duodenum, anterior, multiple	Perforation with peritonitis
12	Davis[3]	22	0	25	50	75	Esophagus and stomach	Perforation (esophagus) with pleural infection
13	Robson[20]	29	15	16	2	33	Esophagus, multiple	Perforation with pleural infection
14	Miln and Ross[14]	32	18	26	0	44	Stomach and duodenum, multiple	Hemorrhage
15	Rankin[19]	4	0	27	0	27	Esophagus	Hemorrhage with minimal perforation
16	Jayesuria and Marsden[11]	6	0	19	0	19	Duodenum, posterior	Hemorrhage
17	Ramsey and Mosquera[18]	78	0	15	0	15	Duodenum, anterior	Perforation and peritonitis
18	Hakuda and Nagasima[10]	5	0	7	0	7	Duodenum, posterior	Hemorrhage
19	Koch and Fischer[13]	68	0	—	18 —	18	Duodenum and stomach, multiple	Perforation (duodenum) and peritonitis
20	Peer[16]	5	0	0	12	12	Duodenum, posterior	Hemorrhage
21	Braithwaite and Beales[2]	52	0	0	5	5	Duodenum, posterior	Survived
22	Hansen[5]	36	0	—	33 —	33	Duodenum	Survived

TABLE II. CLINICOPATHOLOGIC CORRELATION

PREDOMINANT MANIFESTATION OF ULCER	NUMBER OF CASES	PER CENT OF CASES REPORTED	NUMBER WITH WOUND INFECTIONS	AVERAGE DURATION OF SURVIVAL (POST-BURN DAYS)	LOCATION OF ULCERATIONS					MULTIPLE LESIONS
					POSTERIOR DUODENUM	ANTERIOR DUODENUM	STOMACH	ESOPHAGUS	TERMINAL ILEUM	
Hemorrhage	10*	45.4	3	8.5	8	1	1	1	0	2
Perforation with peritonitis	7	31.9	2	31	0	6	6	3	0	5
Ulcer an incidental finding at autopsy	5	22.7	3	11	2	1	2	1	1	5
Total	22	100	8	16.5	10	8	9	5	1	12

*Two patients survived.

The type of complication varied directly with the location of the ulcerative lesion (Table II). In the ten cases in which the patients had a severe hemorrhage, the ulcer was located on the posterior aspect of the first portion of the duodenum in eight, on the anterior aspect of the first portion of the duodenum in one, and in the stomach and esophagus in one. The ulcers of the posterior aspect of the first portion of the duodenum were in the region that is traversed by a major branch of the gastroduodenal artery. In seven cases in which perforation occurred, perforation of the anterior aspect of the first portion of the duodenum occurred in six cases, perforation of the stomach in six, and perforation of the esophagus in three. In five cases there were multiple lesions. Of five cases in which the patient had gastrointestinal ulcerations and died from other causes, ulcerations were located on the posterior aspect of the first portion of the duodenum in two, on the anterior aspect of the first portion of the duodenum in one, in the stomach in two, in the esophagus in one, and in the terminal ileum in one. There were multiple lesions in the gastrointestinal tract in all five cases. Patients who had ulcerations and died from hemorrhage survived for an average of eight and one-half days, whereas patients who died from perforation survived for an average of thirty-one days. The 5 patients who died from causes not related to the ulcerative process survived for an average of eleven days.

DISCUSSION

Twenty deaths have occurred in 600 burned patients treated at Brooke Army Medical Center during the past three years. At autopsy, 5 of the 20 patients who died had gastrointestinal ulcerations. This high incidence is evidence against the general impression that gastrointestinal ulcers after burns are less common now than they were formerly.[8, 9] The true incidence of this complication cannot be assessed because ulcers may occur and heal without evidence of their occurrence.

The pathogenesis of these ulcers remains a subject of controversy, and our clinical data fail to support or argue against the theories that have been proposed. Sepsis[9] and hemoconcentration[4] have been incriminated as important causative factors, but in our series neither of these could be consistently correlated with ulceration. Both adrenocortical hyperactivity and failure[24] have been related to gastrointestinal ulcers. In our series, morphologic changes in the adrenal glands were highly variable and apparently unrelated to the incidence of ulceration. In twelve of the twenty-two cases reviewed, gastrointestinal ulcerations occurred after severe extensive burns, the average area involving 57 per cent, but in the 8 other patients who died, the burns were of very limited extent.

It should be noted that in patients in whom severe massive hemorrhage was the predominant manifestation of ulceration, the ulcer was in the posterior aspect of the first portion of the duodenum, and exsanguination occurred from a major branch of the gastroduodenal artery. An emergency operation was performed in only one of the twenty-two cases reviewed. This patient sur-

vived. Harkins reported six cases before 1942 in which an operation was performed several weeks after the onset of symptoms; in five cases, the patients survived. Although the surgical risk attending emergency gastrectomy in a burned patient who has gastrointestinal bleeding presents a formidable obstacle, surgical intervention must be considered in view of the high fatality rate reported with conservative therapy. In almost every case reviewed, the pathologic description of the ulcerative lesion on the posterior wall of the duodenum revealed an acute ulcer with edema and a minimum of scarring. Subtotal gastrectomy is technically less difficult in acute ulcers of this type than in chronic ulcers. Although multiple lesions of the gastrointestinal tract were present in twelve of the twenty-two cases reviewed, in only 2 of the 10 patients who had severe hemorrhage were the lesions multiple. It would appear that it is wise to assume that the lesion is in the posterior wall of the duodenum and that an emergency operation to control the severe hemorrhage may be indicated if a massive gastrointestinal hemorrhage occurs after burns.

SUMMARY

Harkins, in 1942, reviewed the literature on gastrointestinal ulcerations after burns and reported 117 cases. Since that time, seventeen additional cases have been reported. These cases have been reviewed, and five additional cases have been reported from our experience.

In the review of twenty-two cases, the predominant manifestation of the ulcer was hemorrhage in ten and perforation in seven. In the 5 other patients, there were no symptoms of gastrointestinal ulceration, the ulcerative lesions being incidental findings at autopsy. Most patients who had ulcerative lesions of the gastrointestinal tract after burns did not show any signs or symptoms of the lesion until hemorrhage or perforation occurred. In eight of the ten cases in which the patients had a massive gastrointestinal hemorrhage, the ulcer was located on the posterior aspect of the duodenum over the gastroduodenal artery or one of its major branches. Microscopic examination of the ulcerative lesions usually revealed an acute ulcer with little induration of the edges and a minimal cellular response. The usual time of hemorrhage was between the eighth or tenth day, but in some instances hemorrhage occurred earlier. Perforation of the ulcers usually occurred approximately thirty days after the patient was burned.

It is suggested that an emergency operation may be indicated when a massive gastrointestinal hemorrhage occurs after burns.

ADDENDUM

Since this manuscript was submitted for publication, 7 burned patients have died on our Service. Two of these had large ulcers in the first part of the duodenum similar to those described in the body of the paper.

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BENADRYL HYDROCHLORIDE GIVEN INTRAVENOUSLY TO CONTROL POSTOPERATIVE NAUSEA AND VOMITING

W. R. Warrington, M.D., T. J. Pasquesi, M.D., R. J. Kulasavage, M.D., and E. L. McCawley, M.S., Ph.D., Portland, Ore.

(From the Department of Pharmacology, University of Oregon Medical School)

SEVERAL reports have indicated the usefulness of the antihistamine drugs in the prophylaxis and treatment of motion sickness. These new compounds promise to be of some value in controlling the more severe forms of nausea and vomiting encountered in the surgical patient postoperatively or in other patients for various causes: Both the surgeon and the internist seek better ways to prevent or to arrest emesis, not only for the increased comfort of the patient, but also for his safety and well-being. In the surgical patient, postoperative emetic episodes often threaten the successful outcome of an operation by resulting in (a) obstruction of the tracheobronchial tree by vomitus which may lead to atelectasis or which may initiate pulmonary abscesses; (b) dehiscence of the wound from the exertion of intense retching and (c), in both the surgical and medical patient, excessive fluid loss with dehydration and an altered electrolyte balance.

Even with modern methods of anesthesia, the incidence of postoperative nausea and vomiting still remains high. Waters[1] has reported an incidence of 35.5 per cent of nausea and vomiting following 38,079 operations during which all types of anesthetic procedures were used. Under certain surgical and anesthetic conditions this incidence may be as high as 64 per cent.[2]

In the search for a satisfactory and simple procedure to combat nausea and vomiting, the recent trial of antihistamine drugs has been most promising. Since Gay and Carliner[3] reported, in 1949, that diphenhydramine 8-chlorotheophylline (Dramamine) effectively controlled the nausea and vomiting of motion sickness, oral or rectal administration of this drug has met with some success in the treatment of postoperative vomiting.[2, 4-7] Dramamine is now available in a propylene glycol-benzyl alcohol solution for parenteral use. Early reports of its use in this form show a decrease in both the incidence and severity of postoperative emesis.[8]

For the past two years we have administered intravenously the water-soluble hydrochloride salt of diphenhydramine (Benadryl Hydrochloride Steri-Vials) for the control of postoperative emesis. Several advantages are obtained for this route of administration and this form of the drug. Administering the drug intravenously has the advantage that the antiemetic effect is almost immediate in onset. Moreover, in contrast to oral or rectal therapy, utilization of the drug is complete because there is neither loss of the drug in the vomitus before absorption can take place nor possibility of occurrence

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of irregular absorption of an insoluble preparation from the rectum. Dramamine contains 54.3 per cent of the diphenhydramine base (dimethylamino benzhydryl ether), while Benadryl Hydrochloride contains 87 per cent of the same base. Chinn[9] has shown that the 8-chlorotheophylline portion of the Dramamine molecule, used as such, affords no significant protection in motion sickness, and this observation would probably apply also to its use in post-anesthetic emesis.

METHODS AND RESULTS

The studies undertaken by us in the control of nausea and vomiting may be divided into several phases intended to answer these questions. (1) Can Benadryl be administered prophylactically to prevent emetic episodes associated with induction or recovery of anesthesia? (2) Can Benadryl effectively arrest postoperative nausea and vomiting? (3) What types of emetic problems originating from various clinical causes may be satisfactorily treated with Benadryl?

We found that in order to evaluate the results of intravenous antiemetic therapy particular emphasis must be placed on the reliability and completeness of the reported relief of nausea and vomiting. The fact that special therapy was being administered to the patient was not mentioned to the patient at the time to avoid the factor of subjective relief. The patients' considered answers to our questions were recorded in the charts, and impressions of the attending nurses and interns were included. In addition, patients in adjoining beds were questioned as to the presence or absence of discomfort, appetite, restlessness, and vomiting in the treated patient.

1. *Prophylaxis of Postoperative Nausea and Vomiting.*—Benadryl Hydrochloride in a single dose of 100 mg. was administered intravenously, just prior to induction of anesthesia to 106 patients. Previously, routine preanesthetic medication with 10 mg. morphine and 0.6 mg. atropine had been administered subcutaneously on the wards. The anesthetic procedures were of the usual balanced type, including one or more of the following agents: Pentothal Sodium, ether, nitrous oxide, cyclopropane, ethylene, or spinal procaine. The operative procedures were orthopedic in nature and included, for the most part, open or closed reduction of fractures. The duration of operations varied between 10 and 122 minutes, with an average of 88 minutes.

Twenty-six patients, not given any antiemetic drug, were observed under identical conditions to serve as a control series. Of these, 16 reported nausea, while 13 of them vomited one or more times. Since the incidence of nausea and vomiting in this small control series was similar to that reported by others,[1, 2] we made no attempt to enlarge the number of these patients.

Among the 106 patients given Benadryl prophylactically, there were 6 instances of nausea and vomiting during induction of anesthesia or in the immediate postoperative period. Thirteen additional patients had nausea or vomiting three to twenty-four hours after the administration of the Benadryl. The probable duration of the drug's antiemetic effect is about three hours,

which would explain the recurrence of symptoms. In these patients, additional drug was given during the postoperative period. Thus, a total of 87 of the 106 patients, given Benadryl prophylactically, reported no postoperative nausea or vomiting during the total hospitalization period. The over-all protection against nausea and vomiting provided by the intravenous Benadryl in this series would be 100/106, or 94.5 per cent.

2. *Benadryl Used to Arrest Postoperative Emesis.*—It is apparent that an estimation of the effectiveness of the antiemetic therapy when used preoperatively, as described, is based on a comparison of the incidence of nausea and vomiting in drug-treated and control-patient series. The reliability of interpretation of the results depends on subjecting the treated and control patients to the same conditions. But, when general surgical procedures are involved, widely varying conditions affect the incidence and nature of postoperative nausea and vomiting. Thus, patients on general surgical services were given Benadryl only when an episode of postoperative nausea or vomiting had appeared. They were not given prophylactic treatment with this drug.

A total of 58 patients received one or more intravenous injections (100 mg. of Benadryl Hydrochloride) as a therapeutic measure to control emesis. They had been subjected to the following operative procedures: thoracotomy, 2; cholecystectomy, 10; gastrectomy, 4; mastectomy, 5; thyroidectomy, 8; appendectomy, 15; hysterectomy or curettage, 3; and miscellaneous procedures involving laparotomy, 11. In 54 of the 58 patients (93 per cent) nausea subsided within a few minutes following intravenous injection, and there were no subsequent occasions of vomiting. In the remaining 4 patients, vomiting occurred within one and one-half and ten and one-half hours, although in some of these another injection of Benadryl produced the desired relief. For example, one of these patients, subjected to a laparotomy for ureteral obstruction, required a total of nine injections of 100 mg. each of Benadryl at three- to six-hour intervals to control the nausea and vomiting. Thus, the vomiting of this patient was probably not related to anesthesia, as it persisted for four postoperative days. The effect of Benadryl in controlling nausea and vomiting in this case was an important factor in assisting rapid recovery.

3. *Control of Emesis Associated With General Medical Complaints.*—Benadryl was given intravenously to 16 patients seen on general medical services who had severe nausea or vomiting (Table I). The diagnosis for these patients included: chronic glomerulonephritis, recurrent pyelonephritis, ureteral obstruction, acute gastroenteritis, migraine, abdominal trauma with paralytic ileus, bronchopneumonia, subarachnoid hemorrhage, and neurasthenia. Of twenty-five episodes of vomiting for which the dose of Benadryl given was 100 mg. or more, there were eighteen instances in which relief from nausea and vomiting lasted three hours or longer. As pointed out, this coincides with the expected duration of the drug in high concentration in the blood plasma. With a dose of only 50 mg. there was failure to control emesis in some cases, although successful relief could be obtained when the dosage was increased to 100 mg. Two patients who experienced severe and continuous retching

were relieved only for one to one and three-quarter hours by 100 mg. of Benadryl given intravenously. Since these were patients seen early in our study, a larger dose was not used. On occasion, when the inciting cause seemed to be severe, as much as 300 mg. of Benadryl was necessary before relief was obtained.

TABLE I. THERAPY OF NAUSEA AND VOMITING WITH INTRAVENOUS DIPHENHYDRAMINE HYDROCHLORIDE

PATIENT AND AGE (YR.)	DIAGNOSIS	DOSES OF BENADRYL GIVEN	DURATION OF RELIEF (HR.)	REMARKS
L. C., 43	Chronic nephritis	1	12	Persistent nausea and vomiting; unable to retain food. Sodium Amytal, atropine, and codeine ineffective
M.A.L., 59	Bronchopneumonia	1	Complete	Vomiting caused by Aureomycin
M.D.B., 42	Neurasthenia	6	3 4¾ 4 5½ 4½ ¼	Patient acknowledged voluntary efforts to empty stomach
I.G., 46	Abdominal Buerger's disease	1	1	Retching was almost continuous except for the brief interruption after the Benadryl therapy
K. McD., 36	Migraine	1	6	
H.W., 33	Ureteral obstruction	1	Complete	
E.M., 58	Late syphilis; severe blow to abdomen	1	Complete	
E.W., 88	Subarachnoid hemorrhage	3	12 16 Complete	Muscular twitching until relieved by phenobarbital sodium
E.K., 26	Migraine	1	Complete	Retched for 15 minutes after drug, then slept and awoke well
E.V.S., 57	Acute gastroenteritis	1	Complete	
A.M.E., 66	Chronic pyelonephritis; antral peptic ulcer	6	0 6 2¾ 24 10 1	Gastroenterostomy. Died 7 days later
A.W.R., 32	Acute gastroenteritis	1	Complete	
V.F., 42	Recurrent pyelonephritis	1	Complete	Nausea partly due to morphine
N.B., 17	Pregnancy	1	Complete	
A.L., 75	Acute gastroenteritis	1	17	

SIDE EFFECTS

The major side action of Benadryl is drowsiness. The drowsiness, often leading to sleep, is not undesirable when the patient is in bed. In certain pa-

tients, particularly those with cerebral arteriosclerosis, brief visual hallucinations were reported. These actions on the central nervous system did not interfere with the course or amounts of agents required for surgical anesthesia.

Millett and Henry[6] reported muscular twitchings and convulsions following the use of Dramamine. We also noted muscular twitching in one patient with subarachnoid hemorrhage using 100 mg. of Benadryl intravenously; this was terminated promptly by an intravenous administration of phenobarbital sodium. When Benadryl was again given to this patient twelve hours later, the prior administration of the barbiturate seemed to protect her against this untoward effect. Wyngaarden and Seevers[10] reported that children seem predisposed toward the development of convulsions on antihistamine therapy, and deaths were reported in children under 2 years of age. The youngest patient in our series was 7 years old, and this child did not develop twitchings or convulsions with Benadryl.

We have observed, as reported by Winder and Thomas,[11] that a fall in blood pressure results when rapid intravenous injections of Benadryl Hydrochloride are made in dogs. When a slow rate of injection was used (two to three minutes for 100 mg.) no hypotension occurred; rather, there was a rise of 10 to 20 mm. Hg in both systolic and diastolic pressures. When larger doses of Benadryl were to be used, we diluted the drug either in 500 ml. saline solution or 5 per cent dextrose and administered it by drip over a thirty to forty-five minute period of time. We have given as much as 400 mg. of Benadryl Hydrochloride by intravenous drip to elderly patients with cardiovascular disease with no ill effect other than the expected hypnotic action.

SUMMARY AND CONCLUSIONS

Benadryl Hydrochloride, given intravenously in 100 mg. doses, was administered to 180 patients in an effort to control or prevent nausea and vomiting. The gratifying antiemetic response observed in these patients is an argument in favor of the routine use of Benadryl to control postoperative nausea and vomiting.

The intravenous route of administration increases the reliability of the action of the drug without danger to the patient. Doses of 50 mg. or less of Benadryl are less uniformly effective than 100 mg. or more. This drug is effective in preventing or controlling nausea, with or without anorexia, vomiting, and retching, in a wider range of clinical conditions than heretofore reported.

The major side effect from Benadryl, given intravenously, is drowsiness. Other side effects seen were stupor, brief visual hallucinations, muscular twitching, dryness of the mouth, pain along the course of the vein used for injection, and slight hypotension or hypertension, depending on the rate of injection. These side effects did not affect the course of anesthesia or the postoperative recovery of the patient.

Acknoledgment.—We wish to express our appreciation for the cooperation and courtesy extended to us during the course of this work by the staffs of the Emanuel, Good Samaritan, Portland Sanitarium, Providence, and St. Vincent's Hospitals of Portland, Ore.

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DUPLICATION OF THE ENTIRE COLON, BLADDER, AND URETHRA

MARK M. RAVITCH, M.D.,* NEW YORK, N. Y., AND WILLIAM WALLACE SCOTT, M.D., BALTIMORE, MD.

(From the Department of Surgery and the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore)

THE child who is the occasion for this report was referred to The Johns Hopkins Hospital because of a deformity of the penis and because of life-long abdominal distention. At birth he weighed seven pounds, fifteen ounces, but almost constant diarrhea for the first four weeks of life caused a loss of one pound, ten ounces in weight in six weeks. The diarrhea changed to constipation about the fourth week of life. The child became tremendously distended and remained so thereafter despite special diets and the administration of a variety of daily enemas. From the time the child was 3 or 4 weeks old until the summer of 1948, when he was a little more than 4 years old, he never had a stool except with an enema and he was almost constantly distended. Passage of a rectal tube ten or twelve inches above the anus would relieve the distention a little. The mother was quite positive the rectal tube did no good until it passed at least that far. When the child was 1 year old, a barium enema was performed but the barium would not run into the bowel until the tube was inserted a distance of fourteen inches.

When the boy was 6 weeks old, he became completely obstructed and unusually distended, had no stool for four days, and began to vomit. He was hospitalized, transfused, and eventually relieved without operation. At the age of 2½ years, he had another severe attack of vomiting which was treated at home. He was said to cry frequently with severe abdominal pain. Often large fecal masses were visible and palpable in the abdomen. Bouts of typically cramplike pain recurred from time to time. In June, 1948, when he was a little over 4 years old, the bowels began to move without assistance, but remained just as distended as before. He would have spontaneous stools for four or five days, these gradually decreasing in volume until finally he would fail to defecate for two days, whereupon he would again begin to evacuate spontaneously passing enormous stools on the first day. From the time he was 1½ years old he had, on a number of occasions, suffered a prolapse of the rectum of about two inches. He had become habit-trained only a few months before admission. He had never been able to eat much food at a time and had begun to eat frequent small meals because he became so distended after the ingestion of a small amount of food, becoming hungry again one or two hours after eating. Otherwise his health seemed reasonably good, and he had been bright and active although handicapped by the great distention. It was noted that although he seemed to void adequately, he nevertheless dribbled incontinently in the intervals.

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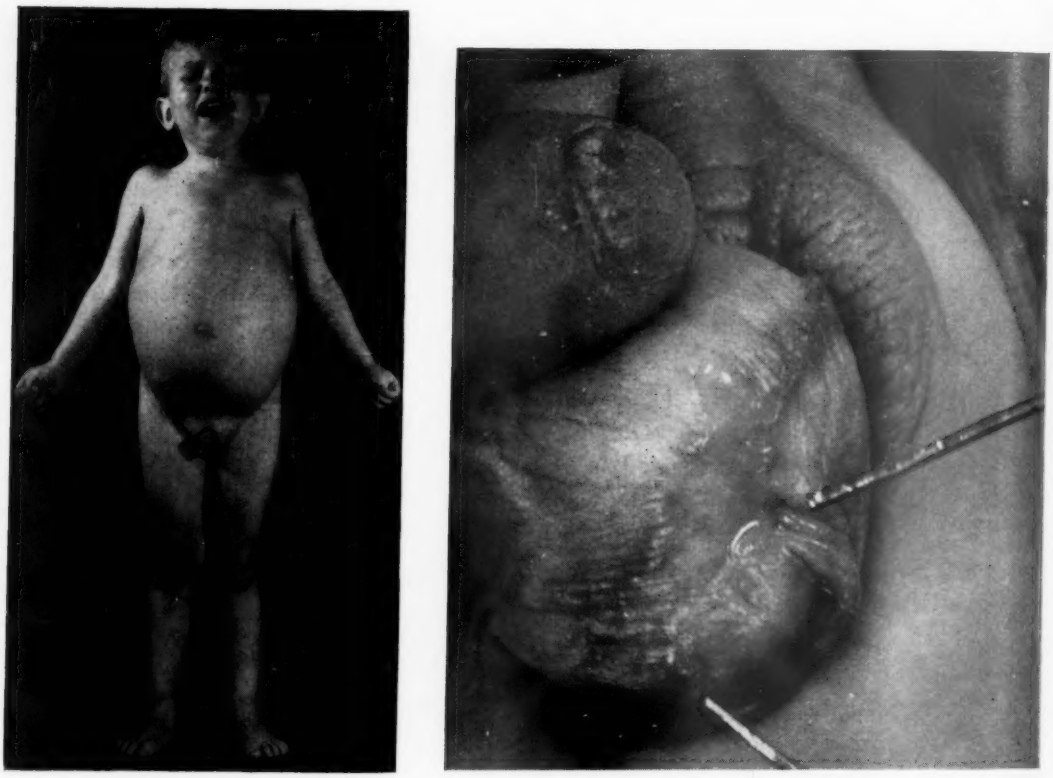
*The Mt. Sinai Hospital.

Physical examination disclosed a little boy of 4½ years with a colossally distended abdomen (Fig. 1, *A*) and a pronounced lumbar lordosis. The abdomen was hugely distended in all directions, and the costal margins flared. Large intestinal loops about four inches in diameter could be seen, and there appeared to be one coursing from the left lower quadrant to the right upper quadrant. Sphincter tone was good but not spastic. The rectum immediately above the sphincter was cavernous. There was no spina bifida.



A. *B.*

Fig. 1.—*A*, F. M. at 4½ years. There is a tremendous distention of the abdomen with flaring of the costal margins. One could frequently see and feel large intestinal loops.

B, Close-up of penis. The lower pointer indicates the urethral orifice within the glans itself. This is the orifice which led to the functioning right bladder. The upper pointer indicates the orifice which is almost in the prepuce. A little turbid urine can be seen around this orifice, and between the pointer and the thumb of the examiner there can be seen the bulge which corresponds to the diverticulum of the urethra.

From the time of birth he had been noted to have two openings in the glans penis (Fig. 1, *B*), the one in the glans proper, and more or less to the right, being the chief site of micturition. Urine passed from this freely when the child voided. The other orifice was a little to the left in a position corresponding to the corona, and here there seemed to be a sort of redundancy of the glans with a peculiar sac of scrotal skin. From this left orifice, urine dribbled from time to time, and in general the child voided very frequently, appeared to have some discomfort when voiding, and was often incontinent. It was felt that he had a congenital malformation of the penis, the nature of

which was not clearly understood at first, and that he had Hirschsprung's disease. An intravenous pyelogram showed dye in the right kidney and ureter, and none on the left. Abdominal films showed a tremendous amount of feces in a huge, dilated loop of large bowel. A barium enema showed a large rectal ampulla with no kinking or narrowing in the region of the pelvic floor. The sigmoid ascended on the right, and it was possible to fill with barium what was thought to be the entire bowel, which was dilated and voluminous. The small bowel did not fill, and what seemed remarkable was that although it was felt that the large bowel was filled to the cecum, there remained a huge loop of intestine which contained feces but no barium (Fig. 1, *C* and *D*). This was puzzling, as was the fact that after four days of constant high colonic irrigations the child was as distended as ever.

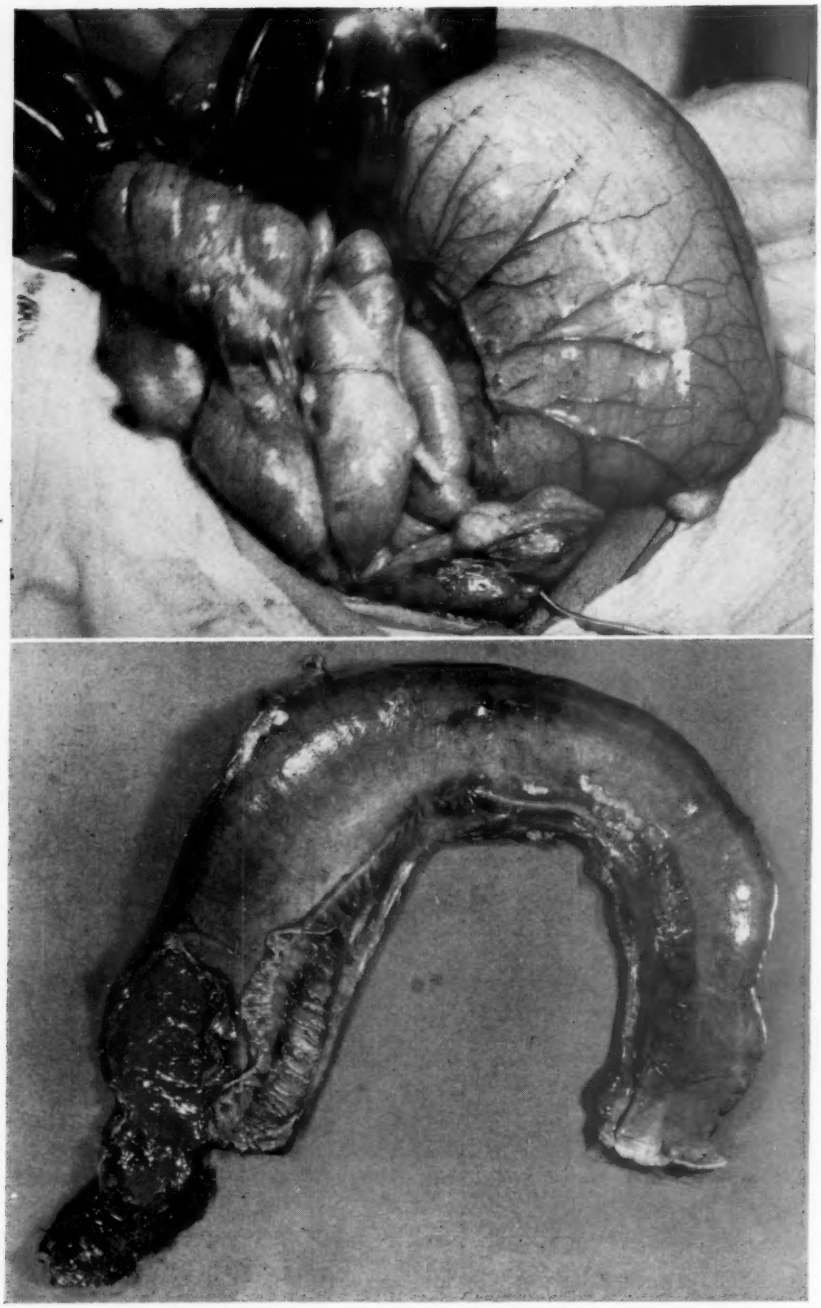
C. *D.*

Fig. 1.—*C,* Roentgenogram of a barium enema. It is possible to trace the rectum and sigmoid distended and displaced by the large feces-filled mass, and then to follow the barium around through the colon to the cecum. This film is actually pathognomonic, but its significance was not appreciated. Actually, an entire normal-appearing colon fills, yet other loops of what appears to be colon are free of contrast medium.

D, In the expulsion film after the barium enema one can, with a little difficulty, trace two parallel loops of bowel, outlined by barium and one distended with air, the latter actually being the reduplication.

It was decided that the intestinal condition, which was diagnosed as Hirschsprung's disease, was the primary one, and that operation should be undertaken. On Nov. 27, 1948, the abdomen was opened through a transverse incision below the umbilicus. The nature of the anomaly was at once

A.



B.

Fig. 2.—*A*, Photograph at operation. The enormous reduplication is seen on the right side of the photograph. The cecum communicates broadly and directly with both the normal bowel and the beginning of the duplication. There is only one vermiform appendix. The clamp just above the symphysis pubis points to an indentation between the domes of the bladder which first suggested that the patient might actually have two bladders.

B, Specimen resected at the first operation. The small normal colon on the inside of the loop is seen to be quite empty as a result of the preoperative preparation, but the great duplication is filled with pasty feces.

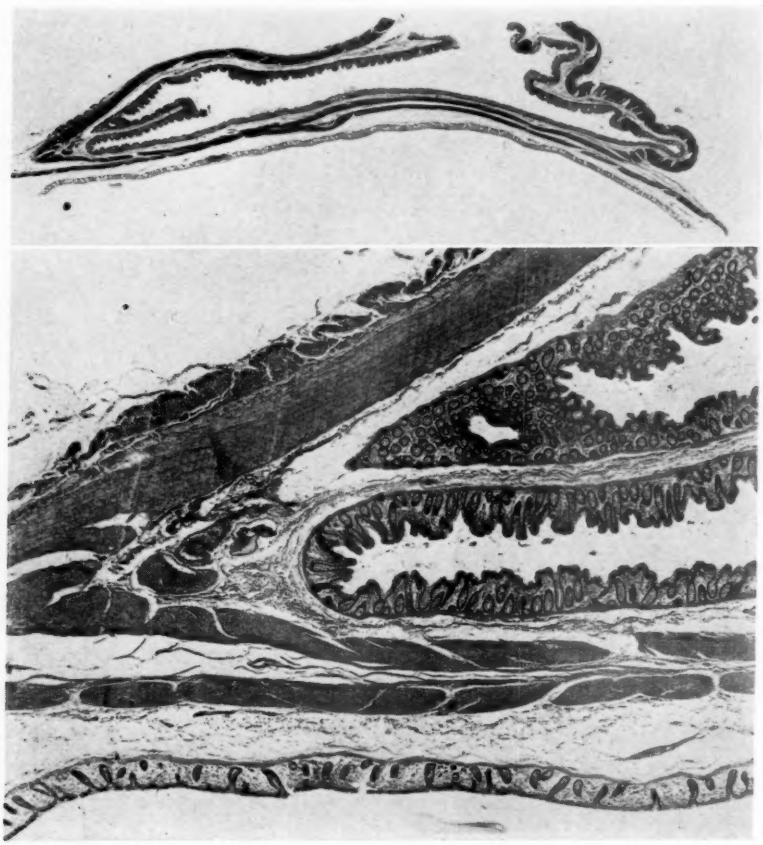
plain. The colon was perfectly normal, but attached to it and intimately adherent was an enormous duplication which looked like a second tremendously dilated and hypertrophied colon (Fig. 2, *A* and *B*). The position of the ileum, ileocecal valve, and appendix at the upper end and the position of the rectal tube passed from below at the lower end definitely distinguished the true colon from the duplication. The duplication was several times the diameter of the normal colon and was hypertrophied and thickened. This thickening increased progressing distally toward the portion of the duplication attached to the rectum and sigmoid, which was five or six inches in diameter, colossally thickened, and hypertrophied. There was a wide communication between the duplication and the cecum amounting, actually, to an uninterrupted continuity of the lumina (Fig. 2, *A*). It was possible to dissect between the two structures for perhaps ten or twelve inches beyond the ileocecal valve, and so to free up and save at least that much of the proximal colon. Distally, it

Fig. 2.—*C*, Cross section of the fixed specimen showing the relative sizes of the normal colon and of the duplication and the broad extent of the fusion between them.

finally proved to be impossible to separate the rectum from the duplication, although we persisted even to the point of perforating the rectum in the attempt. It finally seemed quite plain that if we continued we should only jeopardize the viability of the rectum without effecting a removal of the duplication in this area. We therefore decided to amputate both the rectum and the duplication in the left lower quadrant and to resect all of the proximal duplication and as much of the proximal colon as could not be separated from the duplication. The duplication was transected a few inches beyond the cecum so that a portion of it could serve as an enlargement of the cecum. About twelve or fourteen inches of right colon could be saved. The transverse and descending colons were entirely removed, together with the

enormous duplication. The distal stump of the duplication was now opened, and a great amount of thick, but soft and not inspissated, feces washed out. The entire hand, wrist, and forearm were then passed into the duplication. The rectal tube could be felt lying in the normal rectum and could not be palpated except through the wall of the duplication, so that there appeared to be no communication between the duplication and the rectum. The only communication of the duplication with the bowel appeared to be at the cecum. The proximal colon was brought out as a colostomy at one end of the transverse wound, and the rectum and duplication were brought out through the other end in double-barreled fashion.

D.



E.

Fig. 2.—*D*, Photomicrograph (×3, reduced one-fifth) showing most of the cross section of the opened colon and the adjacent portion of the duplication.

E, Photomicrograph (×20, reduced one-fifth) showing the junction between the duplication and the normal bowel. In the septum between the two, there can be seen a normal mucosa on either side and a submucosa, but only two layers of circular muscle can be seen, with only an occasional strand representing longitudinal muscle. The duplication was apparently covered solely by circular muscle.

The bladder was at least twice as large as one would expect in a child of this size, and it appeared to be bilobed as if perhaps there were a doubling of the bladder as well (Fig. 2, *B*).

The right kidney was in the normal location, and was perhaps a little large for a child of 4½ years. The right ureter could not be seen or felt. The left ureter was greatly enlarged, tortuous, and varicose. It was at least 1 cm. in diameter. The left kidney was a small, rubbery organ about 2 cm. in diameter, almost fused with what appeared to be a normal adrenal. There was nothing else suggestive of a left kidney, and as far as could be determined the right kidney was a single kidney and not a double or horseshoe kidney. It was now felt that the child had a complete double colon, a double bladder, a double urethra, and a left hydro-ureter with atrophy of the kidney caused by pressure from the enormous rectal portion of the duplication upon the ureter at the pelvic brim.

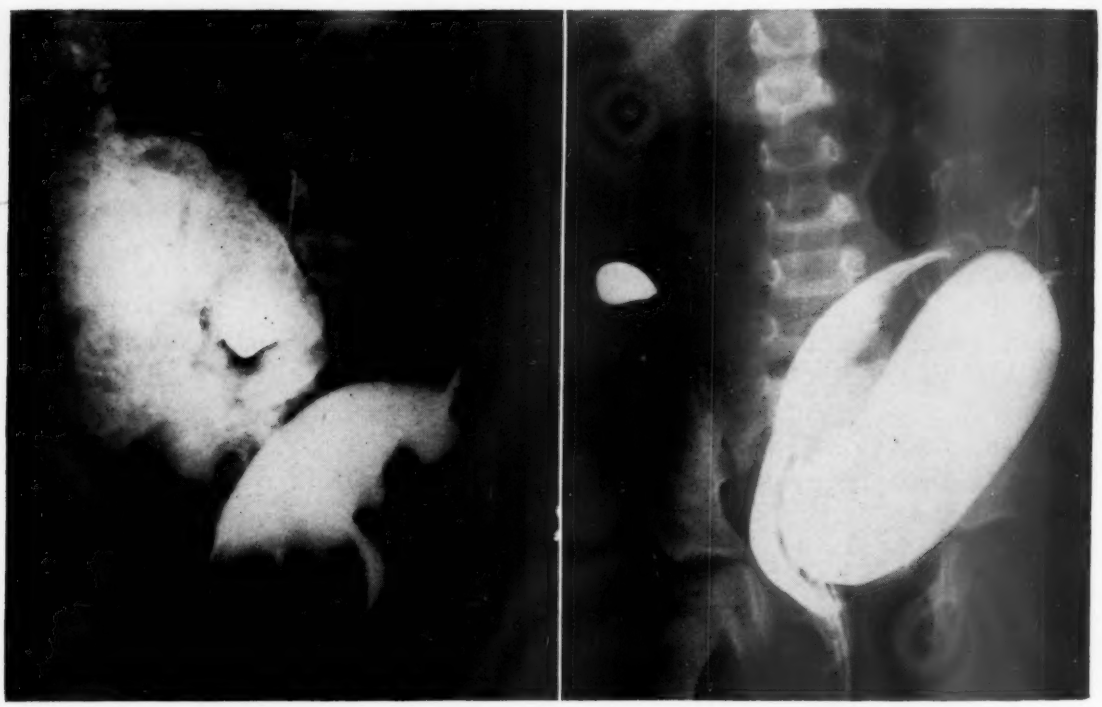
Examination of the resected bowel (Fig. 2, *C*) showed an intimate attachment of the colon proper and the duplication for the entire length of the specimen. The microscopic sections (Fig. 2, *D* and *E*) demonstrated the presence of normal mucosa and submucosa on either side of the common septum. This septum was composed of two layers of circular muscle with only an occasional suggestion of longitudinal muscle. The longitudinal muscular coat of the colon proper did not surround the duplication, which was covered solely by circular muscle.

The child convalesced well after operation except for several bouts of high fever. Re-evaluation of the urologic status showed that the scrotumlike mass of skin on the left side of the duplicated penis actually covered the sac of a diverticulum of the left urethra. Pressure upon this diverticulum expressed 5 to 10 c.c. of thick urine and pus.

The abdomen remained completely scaphoid after the first operation. Repeated roentgenologic investigation of the rectum and of the remaining portion of the duplication failed to demonstrate any communication between the two (Fig. 3). Finally on Dec. 17, 1948, three weeks after the first operation, the abdomen was reopened through the old incision. The rectum and duplication were freed up, and the portion of the duplication not attached to the rectum was freely cut away with the scissors, taking all thicknesses and leaving only the portion of the wall which was fused with the rectum and also the very bottom of the pouch of the duplication which was practically inaccessible. Then, the thin sheet of mucosa and submucosa of the duplication was peeled off the septum between the two colons. The same treatment was accorded the bottom of the duplication in the pelvis. Thus, all of the duplication was removed except a strip of the muscular coat about one inch wide running down the anterolateral wall of the rectum and sigmoid and a cup-shaped area of muscular coat at the bottom of the pelvis (Fig. 4, *A* and *B*). The appendix was removed. The operation had required too much time to permit consideration of an anastomosis at this point.

The patient did well again after this procedure. On Jan. 3, 1949, cystoscopy was performed. The pin-point meatus of the accessory glans on the left was first catheterized with a No. 3 Fr. ureteral catheter. The catheter coiled up in the urethral diverticulum on the left side of the shaft of the penis. This meatus was finally dilated with sounds, and a No. 12 Fr.

panendoscope was introduced. The entire interior of the diverticulum revealed nothing of significance except a minute opening which could not be instrumented but which could be catheterized for about 2 cm. by a No. 3 Fr. ureteral catheter. The catheter could not be passed further than this. On the right side, where there was a larger urethral orifice, a No. 5 Fr. catheter could be passed directly into the bladder. X-ray pictures made after Skiodan had been introduced into the right urethra, demonstrated an asymmetrical bladder with a rounded outline on the right and a straight left border practically in the midline. An attempt to inject the left urethra simply ballooned out the diverticulum. On Jan. 6, 1949, the third operation was



A. *B.*

Fig. 3.—*A*, After the first operation. Barium injected into rectum and into colostomy outlines proximal segment of colon and cecum preserved and the rectal segment.

B, The duplication filled with barium contained in a rubber sheath. The barium injection of the rectum now shows the displacement and obstruction of the rectum by the ballooned blind end of the duplication.

performed through the same incision. The posterior parietal peritoneum was incised, and the left kidney and ureter were exposed. The ureter was again found to be tortuous, varicose, dilated, and hypertrophied, but not so large as it had been at the first operation. The kidney was quite small and firm, about 2.5 or 3 cm. in diameter. There were abnormal vessels entering the surface of the upper pole. The kidney was removed with the ureter. There was sufficient inflammatory thickening around the bladder after the two preceding operations so that we could not now clearly see the differentiation between the two bladders. The left ureter was dissected up almost to the bladder, it was incised, and a catheter was inserted into the bladder through this ureter. Methylene blue injected through a catheter introduced into the

right urethral meatus could not be recovered from the catheter passed into the bladder through the left ureter. Skiodan was injected into the bladder through the catheter in the left ureter, and the ureter was ligated close to the bladder and divided. The two bowel ends were now freed up, freshened with scissors, and anastomosed. X-ray pictures (Fig. 5, *A*) taken immediately after the child left the operating room, after air had been injected into the bladder through the urethral catheter, showed two entirely separate vesical chambers, one on the right connecting with the principal (right) urethra and filled with air and one on the left connecting with the stump of the left ureter and filled with Skiodan, as were the left urethra and its diverticulum. The right bladder contained no Skiodan, and the left contained no air.

The child's convalescence after this operation was uneventful. The mother noticed that for the first time in his life he had no urinary frequency, had good urinary control, and never wet himself. Section of the removed kidney showed it to be involved in pyelonephritis and to contain an abscess at the upper pole. The child was discharged from the hospital on Jan. 17, 1949, having normal bowel movements for the first time in his life. He grew in strength and stature, becoming a normal, healthy, vigorous boy as opposed to his former state as a sickly, constipated semi-invalid with a tremendous, protruding, feces-filled abdomen. In mid-July, 1950, eighteen months after discharge, he became ill with high fever, frequency, dysuria, and the passage of pus from the left urethra. Up to this point he had been entirely free of the old urinary difficulties. At the time of this episode, the diverticulum which had been previously demonstrated in the left urethra was found to be filled with pus and distended to the size of a "plum." He recovered promptly with Aureomycin, but the probability of future attacks made operation seem advisable.

On Sept. 20, 1950, operation was undertaken again. The left bladder was entered through the excision of a small diverticulum which had been previously noted. The complete sagittal septum between the two bladders was excised, together with the left internal vesical orifice. The raw edge so produced was whipped over, and the bladder was closed around a suprapubic catheter. Sections of the septum showed a fairly normal-appearing bladder wall with some chronic inflammation of the mucosa. The suprapubic tube was removed on the tenth day, and the child completed rapid recovery. He was discharged on the seventeenth day after operation, entirely asymptomatic. He has been entirely well since that time.

DISCUSSION

Duplication of the bowel may occur at any level, from the esophagus to the rectum. Generally such duplications form large cysts fused with the adjacent bowel. It is common for such duplications in the colon to communicate with the lumen of the normal bowel, but rare for duplications of the small bowel to show such communications. Duplications of any portion of the bowel are uncommon, but complete duplication of an entire division of the alimentary canal is exceedingly rare. Duplications have usually caused symptoms simply by virtue of their size, presenting either as visible and

palpable abdominal tumors or as causes of intestinal obstruction by compressing the normal bowel. While duplications may be enormous in size, they may also be very small. A recent patient, a 6-month-old infant, had a chronic intussusception due to a duplication 1.5 cm. in diameter at the ileocecal valve. Occasionally, duplications have caused painless intestinal bleeding.

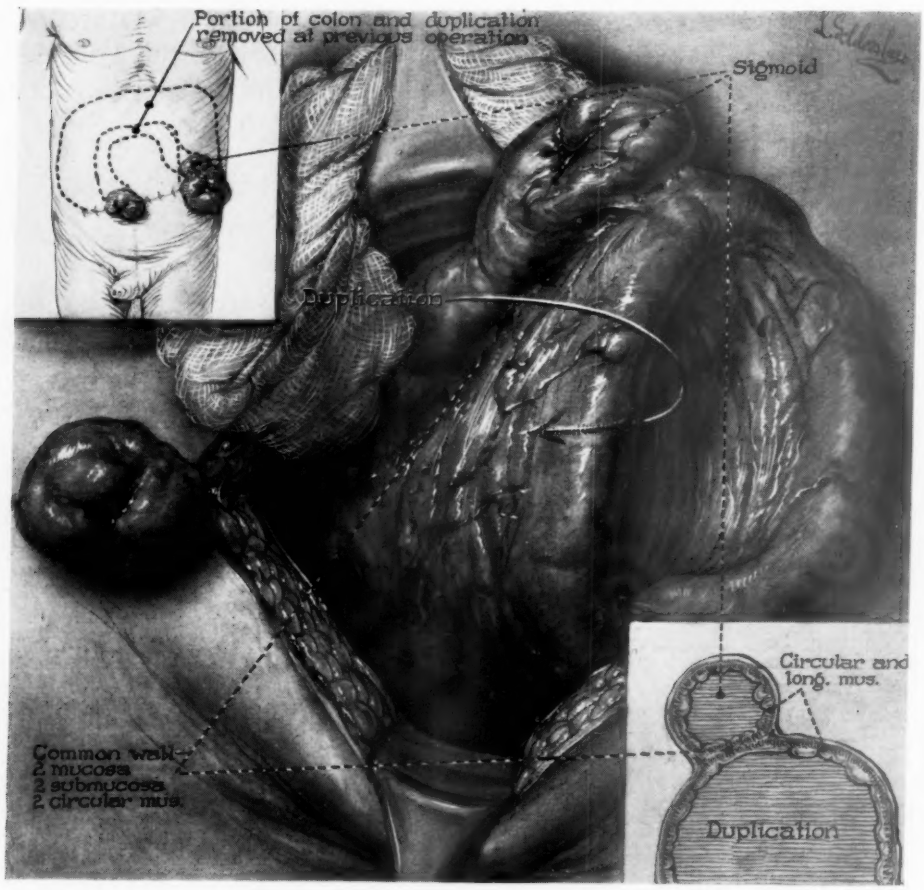


Fig. 4.—*A*, After second operation. The distal portion of the duplication is still enormous in contrast to the remaining portion of the sigmoid. All of the transverse colon, most of the descending colon, and a good part of the ascending colon of both the normal bowel and the duplication had been removed at the previous operation. There is a dense fusion between the duplication and the normal bowel.

Duplications of the colon and rectum, partial or complete, have almost invariably caused symptoms by reason of their distention with feces.[1, 2] This is evident in the present instance. Enemas could be administered only when a tube entered ten to twelve inches or more, that is, when it passed above the rim of the pelvis beyond the point at which the normal bowel was compressed by the feces-packed cul-de-sac of the duplication. The ureter also was obstructed at this level.

Although we have used the term duplication freely in the foregoing paragraphs, it is apparent that this condition of doubling of the colon, bladder,

and urethra must arise by a mechanism quite different from that which gives rise to the lesions formerly called "enteric cysts" or "enterocystomas." The term duplication or reduplication has been widely accepted for these lesions, which are essentially local reminders of a limited embryologic mishap. The present case is one of true doubling or duplication, and detailed analysis of the reported instances[3] points to the origin of such anomalies in incomplete or caudal twinning.

Fig. 4.—*B*, The duplication is cut away from the sigmoid and the rectum, taking all layers of the duplication except in the septum between the two structures where only the mucosa and submucosa of the duplication are removed, leaving the circular muscular coat behind. The same maneuver was employed in the very depths of the pelvis.

We are aware of eighteen other cases of complete doubling of the colon in thirteen male patients and five female patients. Nine of these patients have been operated upon.[4-12] At the time of report ten were dead, eight of them without any operative effort. The causes of death are known in six of the patients who were not operated upon. Three died at ages of several days

to 9 months of chronic intestinal obstruction.[13-15] Two of the deaths occurred in children with untreated omphaloceles which resulted in peritonitis.[16, 17] Two died of unstated causes at 1¾ years and 10 weeks, respectively, but probably of intestinal obstruction.[18-20] One apparently survived to adult life without operation,[21] and one[22] was seen only as a child of 2 years then in good health.

A. *B.*

Fig. 5.—*A*, X-ray picture taken immediately after the third operation. A left nephrectomy has been performed, and dye has been instilled into the left bladder through a catheter passed down the left ureter. At the same time, a catheter passed up through the right (functioning) urethra has been used to inject air into the right bladder. The dye outlines the left ureter (arrow), the left bladder, and the left urethra, while the air outlines the right bladder. There is no communication between the two. At the operating table, methylene blue was injected into the right bladder and could not be recovered by a catheter passed into the bladder through the left ureter.

B, The air in the right bladder has been replaced by injected contrast medium. The two bladders remain perfectly distinct.

There is considerable variety in the operative approaches which have been employed. Most of the operative attempts have been based on the finding that the two colons are closely united and that the duplication communicates proximally but not distally. A second opening has, therefore, generally been made between the two loops at some distal point. In no reported case has the patient been left, as in the present instance, with a single-lumened colon (Fig. 6). The results of these essentially decompressive anastomoses appear to have been satisfactory in the main. Riedel operated upon Grohé's patient, reported in 1900. That patient had a septate vagina with two vaginal orifices, and a normal anus and rectum. The doubling of the colon was complete, even to the presence of two appendices, and the

external orifice of the second colon lay at the posterior commissure. Riedel excised the septum between the two rectums, down to the perineum, dividing the tissues between the two anal orifices. He also excised the vaginal septum and reconstructed the perineum. The child was ultimately continent and asymptomatic.

Fig. 6.—Postoperative x-ray picture. Barium enema eight months after completion of the operation shows a large rectum and a fairly normal sigmoid which is anastomosed to the remnant of the ascending colon which lies in the left lower quadrant. The barium passes readily through the peculiarly shaped cecum to the ileum. The peculiar shape of the cecum is due to the fact that a little of the duplication was deliberately saved in communication with the cecum in order to provide more absorptive surface. The child evacuates normally, has no more constipation or distention. His urinary symptoms (dribbling and incontinence) have been entirely relieved.

The patient of Bar and de Kervilly (1909) died despite a colostomy. Ballance's patient (1930) had an anastomosis performed between the two loops, in the transverse colon. The report was made four years after the successful operation. Asai (1933) performed an anastomosis between the two recto-sigmoid areas with a good result. In Weber and Dixon's patient (1946), an adult, eight to ten inches of the descending and sigmoid colon was resected, the septum was excised at either limit of the resection, and an anastomosis was performed. The result was good. Allard, Ross, and Hopkirk (1949) resected both colons down to the sigmoid, excised the septum between the distal segments and anastomosed the ileum to the sigmoid. The result was good. Brunschwig (1948) transected the duplication near its entrance into the vagina and implanted it into the normal sigmoid, leaving a mucous sac to discharge into the vagina. Aitken (1950) successfully repaired an exom-

phalos in a newborn infant with double terminal ileum, double colon, double clitoris, labia, and vagina. Subsequently the abdomen was explored, but the condition was judged to be unremediable.

Léon Diaz (1951), who has generously allowed us to include his patient, resected all of three colons and implanted the ileum into the anus, with fatal outcome.

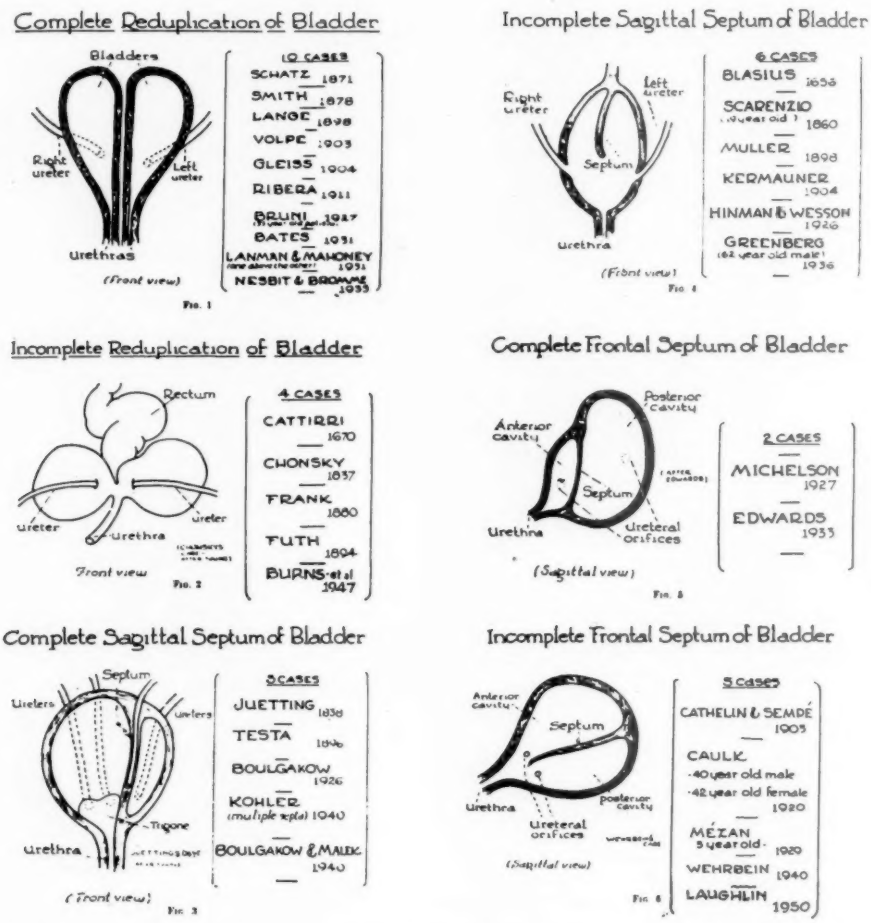


Fig. 7.—Graphic representation of a classification of reported cases of duplication of the urinary bladder. Laughlin, V. C., Derian, G. H., and Boyd, P. F.: J. Urol. 68: 290, 1952, a composite of six figures from Burns, F., Cummins, H., and Hyman, J.: J. Urol. 57: 258, 1947.

Double bladder and double urethra are somewhat more common than double colon.

In 1947, Burns, Cummins, and Hyman[22] reviewed the literature on the subject of duplication of the urinary bladder and set forth their classification. This classification, in graphic form, is reproduced through the kindness of these authors in Fig. 7.

Of the eighteen cases of double colon in addition to our own, there is positive evidence of genital or genitovesical duplication in ten, and in a

number of the other cases it is not clear from the evidence that any study of the genitourinary tract was made. In only one other case in which the colon was double was the double bladder treated operatively, the case reported by Léon Diaz, who excised the septum exactly as was done in the present case with a good result, although this patient succumbed after a later operation (vide supra).

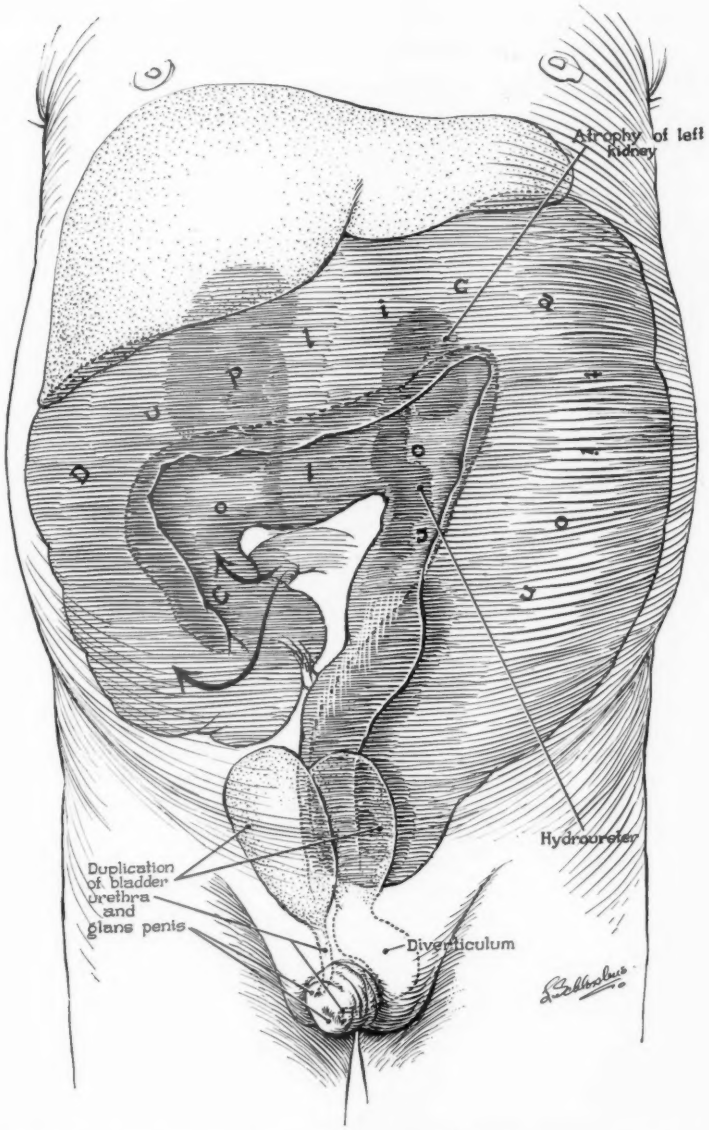


Fig. 8.—Schematic drawing to illustrate the condition found in patient, F. M., at 4½ years. There is one terminal ileum and only one vermiform appendix, but the normal colon at the cecum is continuous with an enormously dilated and hypertrophied duplication which parallels the colon and is densely adherent to it as far as the very depth of the pelvis where it ends blindly. The right kidney and ureter are normal. The left kidney is atrophic, and there is a hydro-ureter on the left. There are two bladders of about equal size. The right bladder empties by its own urethra, through the meatus in the glans. There is a large diverticulum in the urethra leading from the left bladder and a very small meatus almost in the prepuce.

SUMMARY

A case is reported of complete doubling of the colon, bladder, and urethra, presenting with obstinate constipation, distention, and partial urinary incontinence. In a series of operative procedures the entire colonic duplication was removed, the vesical septum was excised, and one urethra was divided. A hydro-ureter and atrophic kidney were removed (Fig. 8). The patient is left with one colon, one kidney, one bladder, and one functioning urethra. He appears entirely well. This type of anomaly, probably representing an incomplete caudal twinning, is to be differentiated from the cystic structures now generally known as duplications and formerly called enteric cysts or enterocystomas. Eighteen other similar cases of true duplication of the colon are reviewed. The mortality of the condition is high, even in the absence of other and graver defects. The duplication generally ends blindly or connects with a small and inadequate fistula. Intestinal obstruction is the chief symptom and requires early relief either by excision of the duplication or by anastomosis of its lower end into the normal rectum or sigmoid. Associated anomalies of the genitourinary tract are extremely common and should be searched for, since operative correction may be required.

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ROENTGEN RAYS AND WOUND HEALING

II. Fractionated Irradiation
An Experimental Study

James J. Nickson, M.D., Walter Lawrence, Jr., M.D., Irene Rachwalsky, D.V.M., and Ella Tyree, A.B., New York, N. Y.

(From the Departments of Surgery and Radiobiology of Memorial Center for Cancer and Allied Diseases)

THE effects of preoperative roentgen irradiation on the healing ability of subsequent surgical wounds have not been well delineated. Recently we reviewed this problem and reported on an investigation in the rat, using a single-dose irradiation method.[1] The present communication concerns a follow-up study in which fractionated irradiation was used in lieu of the single-dose method.

The effect on wound healing of irradiation in the therapueutic range has been shown by others to be a deleterious one. The relationship of this effect to the time interval between the irradiation and the subsequent surgical incision has not been clarified.

In our previous study the abdominal wall of the rat was irradiated (factors: 3 by 2 cm. abdominal field, 100 kv., 6 Ma., 1 mm. aluminum filter, half-value layer 1.8 mm. aluminum, 15 cm. target skin distance, 2,000 r in air) and the healing process of a subsequent surgical wound in this area was followed with tensile strength determinations similar to those reported by Kobak and associates.[2] The irradiated animals demonstrated retarded healing, but final wound strength was in the normal range. Surgical wounds produced three weeks after irradiation healed at almost the same rate as those produced twelve weeks after irradiation despite the fact that the superficial erythema was at its height in the former group. This lack of significant difference between these two groups is contrary to common clinical opinion.

To more closely simulate the clinical situation it was decided to repeat this study in part, substituting a fractionated method of roentgen irradiation for the single-dose method previously used. The result of this follow-up study is the subject of this report.

Method.—Female white Wistar rats weighing 200 to 250 grams were used. Their diet contained 23 per cent protein by weight. Anesthesia for both the irradiation sessions and later operations was obtained with Pentothal Sodium administered in the tail veins. The general procedure was quite similar to that reported in the previous study[1] and will be described only briefly.

The irradiation field was a 3 by 2 midline oval with the superior border of the field determined by the xiphoid process. The factors were: 100 kv.,

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6 Ma., 1 mm. aluminum filter, half-value layer 1.8 mm. aluminum, 15 cm. target skin distance, 500 r in air every two days for four treatments. The control animals were anesthetized and sham irradiated at the time of actual irradiation of the other two groups.

Prior to wound production, the skin was carefully prepared and all materials used at operation were heat sterilized. The standard wounds produced were 2.5 cm., vertical, through-and-through incisions (including peritoneum) within the marked irradiated zone, slightly to one side of the linea alba. These were approximated with three interrupted No. 34 stainless-steel wire sutures through all layers.

Wound strength studies were carried out on small groups sacrificing at intervals of four, six, eight, ten, twelve, fifteen, and twenty days after wound production. Tensile strength was determined after suture removal by the method of Kobak and co-workers,[2] as described in our previous study. This is essentially the determination of the air pressure (in a thin intraperitoneal rubber balloon) required to produce wound rupture.

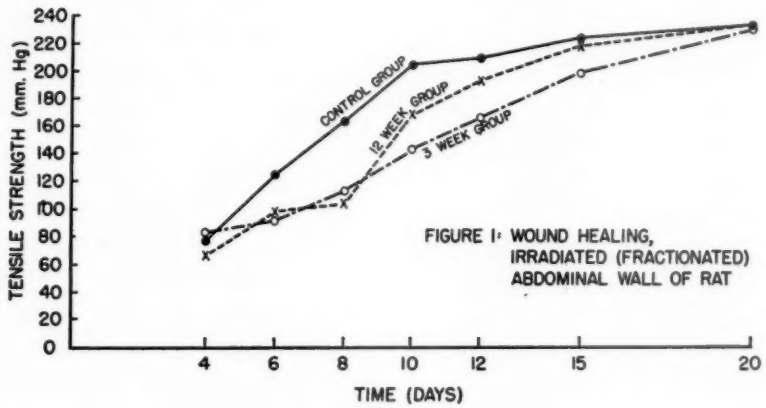

Fig. 1.

In this project only three main groups were studied instead of the previous six groups, and the plasma-protein and histologic studies performed with single-dose experiments were not repeated here. A control group, a three-week irradiation-surgery interval group, and a twelve-week irradiation-surgery group were used. The irradiation-surgery interval represented the time from the mid-point of the eight-day irradiation course to the day of wound production. Each of these three groups represented a total of approximately 100 animals and they were sacrificed after surgery at the intervals described.

The details of the entire procedure have been carefully described in a previous publication.[1]

Results.—The wound described healed per primam without evidence of infection. The tensile-strength findings in the three groups studied are recorded in Fig. 1. Each point on the graph represents the average intraperitoneal pressure required to produce wound rupture in the fourteen an-

imals sacrificed at the time interval indicated. When the wound under examination was able to withstand 230 mm. mercury, other portions of the abdominal wall ruptured instead of the wound area. This healing is, therefore, the highest value that could be recorded. As before, the control series showed a rapid rise in wound strength between the fourth and tenth postoperative days with a slight additional increase in strength during the next five days.

The group of rats in which the fractionated irradiation preceded the standard incision by three weeks demonstrated a slower development of tensile strength than the control animals. The maximum range was not reached until fifteen days after wound production and there was a slight increment in wound strength in the following five days.

TABLE I. TENSILE STRENGTH OF ABDOMINAL WALL WOUNDS IN MILLIMETERS OF MERCURY (PREOPERATIVE FRACTIONATED IRRADIATION)

GROUP		TIME (DAYS)						
		4	6	8	10	12	15	20
Control	Average	77	127	163	203	208	222	230+
	Range	±15	±22	±35	±35	±30	±17	0
3-week x-ray-surgery interval	Average	84	90	112	142	165	198	228
	Range	±25	±27	±35	±35	±30	±37	±4
12-week x-ray-surgery interval	Average	66	97	109	168	192	218	230
	Range	±25	±32	±32	±40	±45	±20	0

The group of rats in which fractionated irradiation preceded surgery by twelve weeks also had delayed healing when compared with the control group. The maximum strength range was reached between twelve and fifteen days, although in the following five days there was a slight additional increment in wound strength. This group demonstrated an increase in rate of wound healing when compared with the three-week group, but this difference was not great, as can be seen graphically in Fig. 1. The actual values for all three groups are recorded in Table I.

Frequent body weight determinations of all rats revealed a slight weight loss in the control group after sham irradiation, but this was regained one week after this procedure. The irradiated animals showed a slightly greater weight loss after the course of irradiation than did the control animals, which were anesthetized but not irradiated. This loss was completely recovered in one to two weeks following irradiation in all but 3 per cent of the total 200 rats. All surgery was performed, then, well after any demonstrated major nutritional effects of the irradiation.

Discussion.—The total dose of radiation administered on four occasions over an eight-day period was 2,000 r (in air). The single-dose study previously reported was performed with a total single dose of 2,000 r (air). As is well recognized, and as expressed in the Strandquist formula, the biologic effect of this amount of x-ray in the fractioned study was less than the same amount given at one sitting. This dose was chosen arbitrarily since there was no way to select a dose in the fractionated study which would be exactly com-

parable to the single dose used previously. In both instances the amount of irradiation given was in a general range comparable to clinical therapeutic dosage, allowing for recovery factors and occasionally higher doses.

The wound-healing curves in these two separate studies show remarkable similarity. Within the limits of the methods used and individual variation in response to irradiation, the three groups bear approximately the same relationship to each other in the fractionated irradiation experiments as in the single-dose experiments. The dose used preoperatively produced a definite retardation in rate of wound healing as determined by tensile-strength measurements. The increase in irradiation-surgery interval from three to twelve weeks produced a definite, but very slight, improvement in rate of wound healing. In both instances the final wound strength was as great as occurred in the controls, although delayed. This reproduces the findings in single-dose irradiation studies.

There is no real reason for us to suspect a different effect on rate of wound healing when preoperative irradiation is given in a fractionated manner rather than as a single dose. Since therapeutic radiotherapy is usually given in a fractionated manner, however, it was felt that confirmation of our earlier results, by using a closer approximation to the clinical plan of treatment, was necessary. It would seem from these studies, too, that there is little to be gained from the healing standpoint by waiting more than three weeks after a course of irradiation to carry out surgical procedures through the treatment area.

CONCLUSION

The effect of local, fractionated roentgen irradiation on healing of a subsequent surgical wound in the rat reproduces the effects noted in single-dose investigations. The rate of healing was retarded in the irradiated animals, but the final wound strength was in the maximum range obtained by the controls. The tensile strength curves showed a slightly greater rate of healing in the group with a twelve-week irradiation-surgery interval than in the group with only a three-week interval. These data seem to strengthen the opinion that there is no practical advantage in delaying surgery more than three weeks after irradiation.

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VITAMIN B_1 DEFICIENCY MIMICKING THROMBOPHLEBITIS IN THE POSTOPERATIVE AND POST-PARTUM PERIOD

BEN EISEMAN, M.D.,* ST. LOUIS, MO.

(From the Department of Surgery, Washington University School of Medicine, and Barnes Hospital)

ONE of the earliest manifestations of vitamin B_1 (thiamin) deficiency is pain and tenderness in the lower extremity.[1] It has been shown that the symptoms are indicative of a peripheral polyneuritis causing lesions which first affect the nerves and muscles of the calf and the anterior tibial group. It is further known[2] that operations, parturition, and lactation increase the need for thiamin. It is understandable, therefore, that a subclinical vitamin B_1 (thiamin) deficiency present prior to operation or delivery may manifest itself as a frank deficiency disease following these procedures, and may result in abnormalities of the leg and calf.

The purpose of this paper is to call attention to the similarity between the signs and symptoms of postoperative and post-partum thrombophlebitis and the clinical picture of thiamin deficiency that may appear during this same period.

CASE REPORTS†

CASE 1.—A male Thai laborer (Naradhivas Hospital No. 661-2495) eight days following an uneventful herniorrhaphy developed bilateral calf pain and tenderness accompanied by swelling of the calf muscles and a positive Homans' sign. Knee and ankle jerks were exaggerated at first but by the seventh day of thiamin therapy they were normal. There was a tachycardia of 100 per minute at the onset of the calf tenderness. Calf pain had disappeared six days following the administration of thiamin.

CASE 2.—A Thai farmwoman (Naradhivas Hospital No. 737-2495) eighteen days following a normal delivery developed pain, tenderness, and swelling of the calf muscles bilaterally. Homans' sign was positive, and knee jerks were absent bilaterally. Calf pain and tenderness diminished within a few days but did not disappear until parenteral thiamin had been administered for fourteen days.

CASE 3.—A Thai housewife (Naradhivas Hospital No. 754-2495) thirty days following normal delivery and lactation developed swelling and tenderness in the calf of the leg. Homans' sign was negative, pulse was normal, and knee jerks were markedly diminished. Ten days following the administration of thiamin the calf pain had disappeared.

CASE 4.—A Malayan housewife (Naradhivas Hospital No. 20-2496) developed calf swelling and tenderness, a positive Homans' sign, and a tachycardia of 120 per minute seven days following a cesarean section. Knee jerks were diminished. After she had received thiamin parenterally for two days the calf pain and swelling disappeared.

Discussion.—These cases are typical of a well-recognized syndrome in Southeast Asia where subclinical thiamin deficiency and frank beriberi are common clinical entities. Physicians in this part of the world recognize that

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*At present, Associate Professor of Surgery, University of Colorado School of Medicine, and Chief of Surgical Service, Veterans Administration Hospital, Denver, Colo.

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their patients frequently develop symptoms of thiamin deficiency during the immediate postoperative or post-partum period, and take it for granted that pains appearing in the leg and calf at that time are most frequently caused by thiamin deficiency. It is their universal practice to administer thiamin in large amounts to these patients, and amelioration of symptoms usually results.

The signs of early thiamin deficiency as illustrated in the cases described are due to peripheral neuritis secondary to demyelination of the peripheral nerve sheaths.[3] It has been shown that such signs appear in the muscles most in use prior to and during the period of vitamin lack,[4] thus explaining the early involvement of the calf and leg muscles. Tenderness is present over the involved nerve trunks as well as over the muscles which these nerves supply.[5] It is understandable, therefore, that tenderness in the calf is present in early thiamin deficiency and that a positive Homans' sign may be elicited.

Wenckbach[6] has described the "curious hardness and swelling of the calf muscles" associated with beriberi peripheral neuritis and has suggested that this is due to an accumulation of extra- and intracellular fluid in the area of involvement. Although such swelling has been noted on occasion it does not always appear to be a prominent feature of early thiamin deficiency, at least in areas where so-called "wet" beriberi is uncommon. Another early manifestation of thiamin deficiency is a slowly progressing tachycardia. Later, however, bradycardia develops.[7]

It is clear that early thiamin deficiency can result in swelling and tenderness in the legs and calves, a positive Homans' sign, and tachycardia. Appearing, as this may, in the postoperative or post-partum period when thrombophlebitis also occurs, the differential diagnosis between the two conditions may be difficult.

Thiamin deficiency causes spontaneous calf pain and tenderness in the postoperative period, but other evidence of inflammation, as may occur with thrombophlebitis, is lacking. Dolor and tumor may be present with thiamin deficiency; calor and rubor are seen only with thrombophlebitis. Unfortunately, during the early stages of thrombophlebitis and phlebothrombosis these two clinical signs of inflammation also may be absent.

Enlargement of the circumference of the calf may occur in thiamin deficiency, but it is usually not as prominent a feature as in most cases of thrombophlebitis. Phlebothrombosis may show very little in the way of calf enlargement during the earliest stages of its development, and a diagnosis is often made and treatment begun before a marked difference in calf diameter has become manifest.

The tachycardia secondary to thiamin deficiency may appear gradually, whereas that secondary to thrombophlebitis is sudden in onset, although evanescent in character. This may afford a supportive point of differentiation.

When reflex changes occur secondary to thiamin deficiency, recognition of the etiology of calf pain is obvious, but depression of the knee and ankle jerks are not always among the earliest signs of such a picture. In the cases

herein described and in others observed, the reflexes of the lower extremities were variably affected and could not be relied upon to establish the diagnosis of early beriberi or to rule out this condition.

The most helpful differential diagnostic point between these two syndromes is the clinical response to large doses of thiamin. In the usual case of calf tenderness secondary to thiamin deficiency appearing for the first time in the postoperative period the patient will respond to adequate doses of thiamin. Pain and tenderness disappear within a few days in the cases where definite thiamin deficiency has not previously been present. This observation is in agreement with Blankenhorn[8] who has noted that "there is a direct correlation between a short duration of symptoms and a short period of recovery." Other neurological signs such as reflex changes and muscle weakness respond much less rapidly than do leg pain and tenderness.

In the management of the postoperative or post-partum patient who develops leg pain and tenderness and a positive Homans' sign without cyanosis or swelling or peripheral cutaneous vascular engorgement, the physician must make a practical choice of therapy. Most such patients will subsequently be found to have thrombophlebitis but, if nutritional deficiency is seriously suspected, it might be warranted to withhold therapy aimed at the management of obstructive venous disease and to give large doses of thiamin for a few days as a therapeutic trial.

Subclinical thiamin deficiency in the United States is by no means an uncommon finding[9] although frank beriberi is usually noted only in alcoholics or in persons who follow food fads.

At this time, when the medical profession in the United States is sensitive to the appearance of thrombophlebitis and phlebothrombosis, it would not be surprising if an occasional postoperative or post-partum patient suffering from leg tenderness secondary to thiamin deficiency were diagnosed as having venous obstructive or inflammatory disease. The clinician must be alert to the differential diagnosis of the two conditions, the one so easily treated by thiamin, diagnosis of the other obligating prolonged treatment with anticoagulants or surgery.

SUMMARY

1. The similarity between postoperative thrombophlebitis and the postoperative appearance of calf pain and tenderness secondary to thiamin deficiency has been emphasized.

2. Cases of such calf pain and tenderness, appearing in the postoperative and post-partum period and caused by thiamin deficiency, have been presented.

3. The differential diagnosis and management of the two conditions has been discussed.

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THE EFFECT OF SYMPATHECTOMY ON EXPERIMENTAL FROSTBITE IN THE DOG

JEROME HAROLD KAY, M.D., AND TIMOTHY S. HARRISON, M.D., BALTIMORE, MD., AND GEORGE D. ZUIDEMA, M.D., BOSTON, MASS.

(From the Department of Surgery of the Johns Hopkins University and Hospital)

THE following studies were undertaken in order to determine the effect of early sympathectomy on experimental frostbite in the dog.

METHOD

Mongrel dogs, weighing seven to eleven kilograms, were anesthetized with pentobarbital sodium given intravenously. The fur of both hind extremities was clipped closely to a point 4 cm. above the knee and the extremities were immersed in a freezing solution. The solution was similar to that described by Fuhrman and Crismon.[1] One liter contained 425 ml. of ethylene glycol, 425 ml. of water, and 150 ml. of 95 per cent ethyl alcohol. The temperature was lowered by the use of dry carbon-dioxide ice. A double chamber was used; the animal's legs were placed in the solution in the inner chamber and the outer chamber contained the solution and dry carbon-dioxide ice. During immersion the solution in the inner compartment was stirred continuously.

Both posterior extremities were immersed simultaneously when the temperature in the inner chamber was between −40° and −50° C. After fifteen to thirty seconds the extremities were frozen solid. The extremities were removed after ten to fourteen minutes and at this time the solution was 5° to 10° C. warmer. Using aseptic technique a right or left lumbar sympathectomy was performed through an abdominal incision within three hours of the time of freezing. Two or three ganglia and the intervening nerve trunk were removed. The identity of the sympathetic chain was confirmed histologically. All dogs were observed daily for a period of at least three weeks.

RESULTS

Thirty-five dogs were used in this study and of these 10 were unsatisfactory because of inadequate freezing or immediately postoperative deaths.

In 25 dogs frostbite was severe enough to produce leg ulcers of varying size and extent. The area of ulcerated skin and subcutaneous tissue was taken as an index of the severity of tissue destruction resulting from freezing.

In 10 dogs there was no significant difference in the size or extent of ulceration of the two extremities. In 7 dogs the ulceration was more extensive on the side of sympathectomy. In 3 this was very pronounced and in 4 there

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was only a slight difference. In 8 dogs ulceration was more extensive on the unsympathectomized side; this difference in tissue destruction was slight in 5 dogs and severe in 3.

DISCUSSION

Sympathectomy within a few hours after exposure to cold, or after longer periods of time, has been frequently suggested and performed on the theoretical grounds that improvement of blood supply to the frozen extremity would lessen the extent of tissue damage. Such clinical impressions, although numerous, have been based on suggestive and inconclusive evidence. Shumacker and Lempke[2] found that sympathetic denervation has a beneficial effect on some of the late sequelae to frostbite. LeRiche,[3] Davis,[4] and Burdenko[5] have suggested that sympathetic block early in the treatment of frostbite may be effective.

Previous experimental approaches employed in the evaluation of the effect of sympathectomy have yielded conflicting results. This is probably due in large part to the diversity of techniques and animals used. Roden[6] performed periarterial sympathectomy in the anesthetized rabbit by touching the femoral artery with 30 per cent phenol. He found that unilateral sympathectomy one hour after freezing of the hind limbs produced increased edema and permanent loss of tissue which did not occur in the other (nondenervated) foot. Denervation two hours later seemed to have no effect.

Kreyberg[7] studied the effect of removal of the right superior cervical ganglion on cold injury to rabbits' ears produced by direct application of solid carbon dioxide. He concluded that the sympathectomized tissue showed a more rapid and abundant development of edema but that final damage was not altered. Arena[8] stated that sympathetic blockade with tetraethylammonium chloride had no effect on tissue loss of rabbit legs which had been frozen by immersion in a freezing solution. Our results are similar to those of Kreyberg and Arena since we also found that lumbar sympathectomy had no consistent effect on the severity and extent of destruction of tissue of dogs following freezing.

SUMMARY

Unilateral lumbar sympathectomy was performed in 25 dogs within three hours after experimentally freezing both posterior extremities. The comparative degree of tissue destruction in the two legs was observed for a period of three weeks. In 10 dogs there was no significant difference in the degree of ulceration of the two sides. In 7 dogs the ulceration was more extensive on the side of sympathectomy. In 8 dogs ulceration was more pronounced on the contralateral side. In the dog, immediate sympathectomy does not appear to influence the degree of tissue destruction occurring as a result of experimental frostbite.

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THE EFFECT OF N-ALLYLNORMORPHINE* ON THE CHOLEDOCHAL SPHINCTER ACTION

HERBERT SCHAPIRO, M.S., AND JOHN M. BEAL, M.D., LOS ANGELES, CALIF.

(From the Surgical Service, Wadsworth Hospital, Veterans Administration Center, and the Department of Surgery, University of California at Los Angeles)

RECENT studies have demonstrated that n-allylnormorphine, which is an antagonist of morphine, produces an inhibition of gastric and intestinal motility. It appears to be effective in overcoming the intestinal spasm produced by morphine as well as in affecting spontaneous motility.[1] Because morphine is known to cause a marked spasm of the choledochal sphincter,[3, 7] a study of the effect of n-allylnormorphine on the action of the sphincter of the common duct was made.

METHOD

Five adult male patients from the Surgical Service of Wadsworth Hospital, Veterans Administration Center, Los Angeles, were studied. All patients had choledochostomy tubes and were studied in a fasting state one to three weeks after choledochostomy.

A sterile Y tube was attached to the choledochostomy tube. One end of the Y tube was connected to a recording device.[2] The other end was attached to a perfusion solution by means of an ordinary intravenous set. The number of drops of perfusion fluid flowing through the set was counted visually and recorded. Sterile Ringer's or normal saline solution was used for intraductal perfusion. The flask was maintained at a uniform height for the studies (approximately thirty-six inches above the common duct).

Whenever it was possible, the duodenum was intubated with a single balloon in order to obtain simultaneous motility tracings. The balloon was inflated with 15 c.c. of air and attached to the recording apparatus.

The perfusion fluid was allowed to flow at a uniform rate during a control period of twenty or thirty minutes. Pulse readings were taken and recorded at regular intervals. Respiratory rate and amplitude were recorded by use of a chest pneumograph.

Increased common duct pressure was produced by intravenous injection of 10 mg. of morphine. This rise in intraductal pressure was accompanied by a decrease in the rate of flow of the perfusion solution.

The study was divided into two parts. In the first part, n-allylnormorphine was administered after the injection of morphine. In the second part, n-allylnormorphine was given prior to the administration of morphine.

RESULTS

Lowering of Increased Common-duct Pressure Produced by Morphine Stimulation.—Five milligrams of n-allylnormorphine injected intravenously five

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*N-allylnormorphine supplied through the courtesy of Merck and Company, Inc., Rahway, N. J.

to ten minutes after the administration of morphine caused a prompt decrease in intraductal pressure in the two cases studied (Fig. 1).

The pressure in the common duct rose in a manner essentially paralleling the increase in duodenal tone following the intravenous administration of morphine. The injection of n-allylnormorphine was followed by a prompt return of the duodenal tonus to the control period level. There was a coincident fall of pressure in the common duct, but it was noted that this pressure remained somewhat above the level of the control period, and the rate of flow as measured in drops of the perfusion fluid per minute also remained below the control rate.

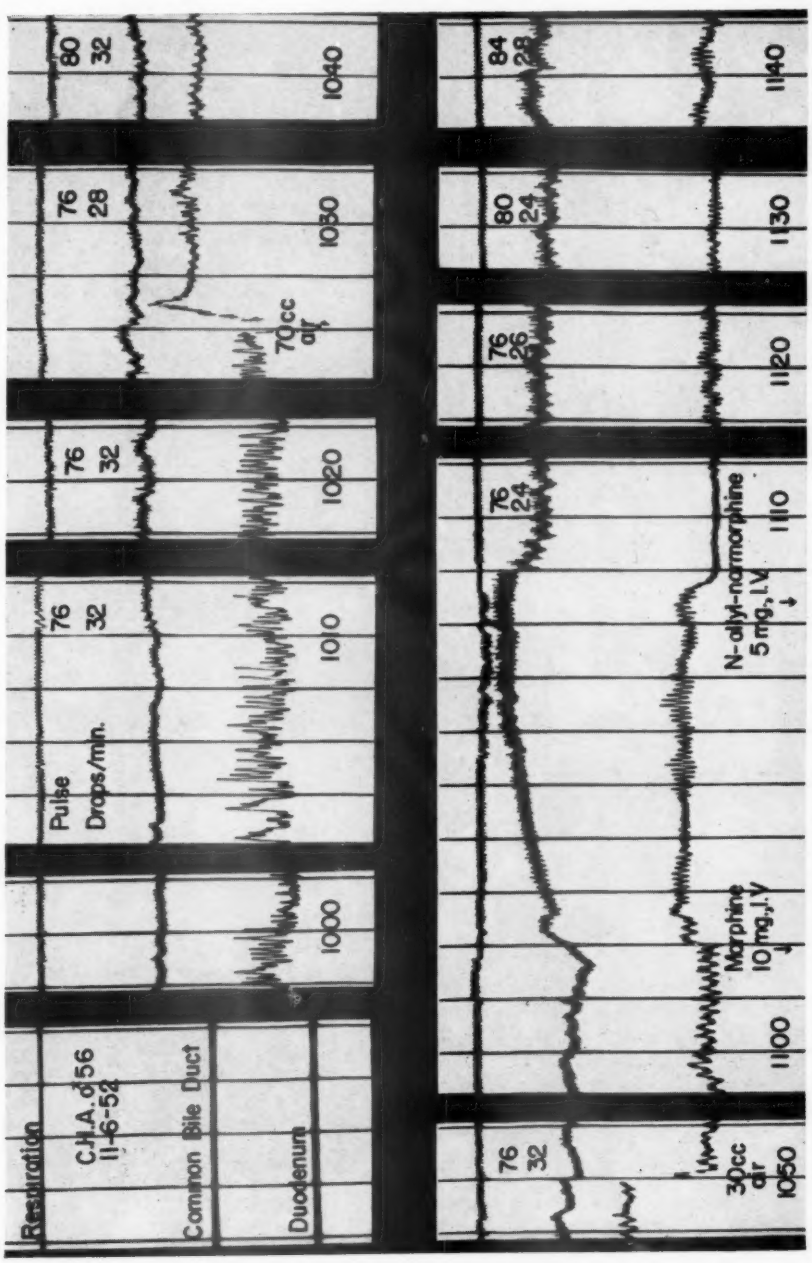

Fig. 1.—Tracing showing decrease in intraductal pressure after the intravenous injection of 5 mg. of n-allylnormorphine five to ten minutes after the administration of morphine.

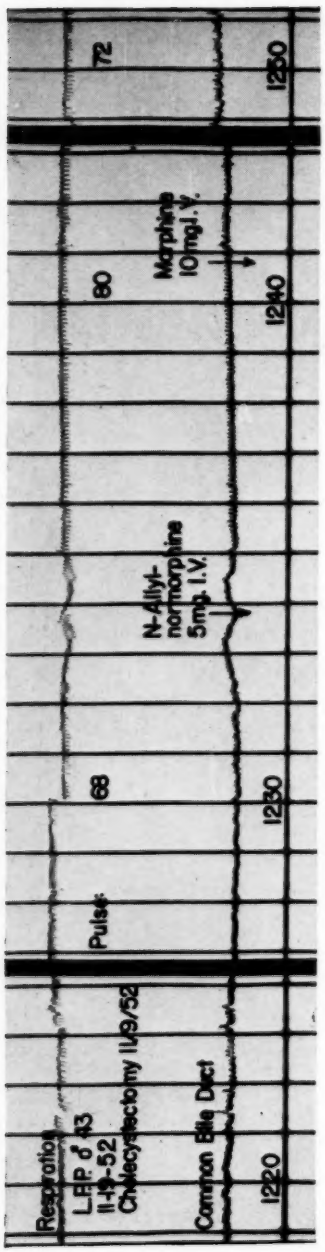

Fig. 2.

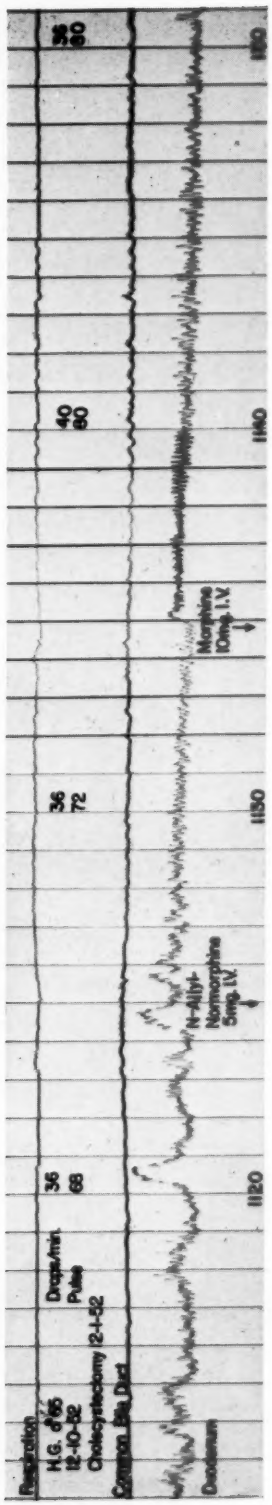

Fig. 3.

Figs. 2 and 3.—Tracings showing prevention of the characteristic rise in intraductal pressure when 5 mg. of n-allylnormorphine was injected intravenously five to twenty minutes before the administration of morphine.

Inhibition of Increased Common-duct Pressure.—In the three cases studied, 5 mg. of n-allylnormorphine injected intravenously, five to twenty minutes before the administration of morphine, prevented the characteristic rise in the intraductal pressure (Figs. 2 and 3).

In one case (Fig. 2) there appeared to be a slight increase in common duct pressure ten minutes after the morphine had been given, but the rate of flow of the perfusion fluid was not significantly altered. In the second case, a definite though minimal increase in duodenal tonus was not reflected in the common-duct pressure.

DISCUSSION

These studies support previous observations that n-allylnormorphine antagonizes the stimulation of motor activity produced by morphine in the gastrointestinal tract.[1] In the three cases studied, the injection of n-allylnormorphine prior to the administration of morphine almost entirely abolished the usual effect of morphine upon gastrointestinal motor activity. The failure of the common-duct pressure to return to the level of the control period has been interpreted as evidence that the choledochal sphincter is capable of action independent of the duodenal musculature.[7] The effectiveness of n-allylnormorphine in preventing the usual response of common-duct pressure to morphine stimulation is not clearly understood.

The mechanism of action involved apparently differs from that of anticholinergic drugs (atropine, Banthine) which does not prevent the response to morphine.[7]

SUMMARY

Studies of choledochal pressure were made on five patients who had choledochostomy tubes. The effect of n-allylnormorphine on choledochal pressure before and after morphine stimulation was observed. When n-allylnormorphine was given after the increase in intraductal pressure had been produced by morphine, there was a prompt decrease in common-duct pressure. When the n-allylnormorphine was given before the morphine, the characteristic rise in intraductal pressure was not seen.

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THE INFLUENCE OF INANITION ON THE UTILIZATION OF A LOW CALORIC-AMINO ACID MIXTURE GIVEN INTRAVENOUSLY

M. D. Pareira, M.D., E. J. Conrad, M.D., and R. Elman, M.D.,
St. Louis, Mo.

(From the Surgical Metabolism Division of the Homer G. Phillips Hospital and the Department of Surgery, Washington University School of Medicine)

WHEN the total diet fails to meet the full caloric needs, it has been stated, dietary protein cannot be retained for tissue synthesis.[1-3] But it has also been observed that considerable, though not maximal, protein utilization can be achieved on a low caloric intake.[4, 5] A possible explanation of the difference in these observations lies in a difference in the state of the tissue protein stores of the subjects under study. For example, Allison[6] has shown that normal dogs will go into negative nitrogen balance on a low-caloric diet containing protein, whereas a depleted dog will be in positive balance on the same intake. Cox, Ellingson, and Mueller[7] have shown that protein-depleted rats are able to build protein tissue on a low-caloric diet, whereas well-nourished rats fed the same ration utilize a much smaller part of the dietary nitrogen for tissue synthesis.

The claim that nitrogen balance cannot be achieved on a low caloric intake is a generalization which ignores the fact that nitrogen balance is not a fixed phenomenon, but varies in degree and in response to many factors. In the present paper we want to show that one of these factors is the state of nutrition in that, unlike the normal patient, patients suffering severe inanition show a strongly positive nitrogen balance on a low caloric intake.

METHODS OF STUDY

Subjects of the present study were thirteen extremely undernourished patients in whom the body weight had declined to an average of 65 per cent of the previous normal weight. The inanition in all cases was due either to the uncorrected anorexia of disease or to mechanical inability to eat. None of the patients had suffered protein losses other than as a result of diminished intake, and in none was there azotemia. The periods of study consisted of three consecutive days during which the patient was given intravenously, as the sole intake, 2 L. of 5 per cent amino acid mixture (Amigen) and 5 per cent glucose (ten patients), or 5 per cent Amigen and 10 per cent glucose (three patients) per twenty-four hours, providing a daily intake of 12.6 Gm. of nitrogen and 400 or 800 nonprotein calories, respectively. On the day preceding and the day following each experimental period, 2 L. of 10 per cent

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glucose providing a total of 800 calories was infused at the same rate. In three patients the same procedure was repeated after from two to four weeks of dietary repletion. Twenty-four hour urines were collected during each experimental period, and analyzed for total nitrogen and creatinine content. Daily blood nonprotein-nitrogen determinations were made before, during, and after the experimental periods.

FINDINGS

All thirteen patients, as studied initially (Table I), were in positive nitrogen balance during the administration of the amino acid-glucose mixture. The mean for the entire group was +5.5 Gm. of nitrogen per day; the minimum positive balance was 1.5, the maximum 8.1 Gm., and the standard deviation 2.0. The efficiency of nitrogen utilization by these patients is evident upon noting the striking similarity in the level of nitrogen excretion during the administration of amino acids and glucose. Indeed, in Cases 1, 5, and 8 the nitrogen excretion upon infusing 12.6 Gm. of amino acids with glucose was actually less than the output during the control days on glucose alone. The largest increase in nitrogen output during the infusion of amino acids occurred in Case 7, but even here the control output of nitrogen on glucose alone was 7.7 Gm., which rose to 11.1 Gm. during the administration of the amino acids and glucose.

Although there is considerable variation in the degree of positive nitrogen balance, scrutiny revealed no correlation with the variations in "normal" weight or weight loss. This does not mean that there is no relation between the degree of protein utilization and the state of protein depletion, but merely that the body-weight loss alone, involving as it does adipose tissue, protein tissue, and body water, gave no information as to the original proportion of each, and as to their relative losses after depletion. It will be noted, however, that the nitrogen utilization in the three patients who received 800 carbohydrate calories was the same as in those who received 400 carbohydrate calories. It would have been expected that there would be an increased nitrogen utilization on the higher carbohydrate intake. On the other hand, in view of the excellent degree of positive nitrogen balance, it does not seem likely that better utilization would have resulted at higher caloric intakes as, for example, has been reported in observations by Ellison and associates,[8] whose findings will be referred to again later. Blood nonprotein nitrogen levels in all patients studied were within normal range and are not recorded. Moreover, they remained within this normal range throughout the experimental period.

The findings in the three patients (Cases 11, 12, and 13) who were subjected to the same experimental procedure following partial repletion, which was carried out by hyperalimentation with tube feeding, are shown in Table II. Here it may be seen that there was a marked diminution in the degree of nitrogen balance as compared to the findings in the prerepletion state. However, the nitrogen losses in these patients on the adjacent periods of glucose

TABLE I. WEIGHT- AND NITROGEN-BALANCE DATA ON THIRTEEN MALNOURISHED PATIENTS GIVEN INTRAVENOUS INFUSIONS OF 12.6 GM. OF NITROGEN AS AN AMINO ACID MIXTURE (AMIGEN) PLUS 400 OR 800 CARBOHYDRATE CALORIES PER TWENTY-FOUR HOURS FOR THREE DAYS (PRECEDED AND FOLLOWED BY ONE CONTROL DAY DURING WHICH WERE INFUSED 800 CARBOHYDRATE CALORIES PER TWENTY-FOUR HOURS)

PATIENT	"NORMAL" WEIGHT	PRESENT WEIGHT (KG.)	PRESENT WEIGHT IN PER CENT OF "NORMAL"	DAILY NITROGEN BALANCE ON 800 CARBOHYDRATE CAL. ALONE (GM.)	DAILY NITROGEN INTAKE (GM.)	DAILY NITROGEN OUTPUT ON 400 CARBOHYDRATE CAL. (GM.)	DAILY NITROGEN OUTPUT ON 800 CARBOHYDRATE CAL. (GM.)	DAILY NITROGEN BALANCE (GM.)
1. J. C.	57.2	36.6	64	−7.2	12.6	4.5		+8.1
2. G. S.	67.3	50.5	75	−9.0	12.6	10.5		+2.1
3. L. B.	78.2	56.0	71	–	12.6	7.8		+4.8
4. M. I.	67.3	41.7	62	−4.1	12.6	6.9		+5.7
5. D. S.	60.0	35.4	59	−5.8	12.6	5.2		+7.4
6. L. C.	66.4	40.4	61	–	12.6	8.2		+4.4
7. N. Y.	75.0	48.0	64	−7.7	12.6	11.1		+1.5
8. N. B.	65.4	49.1	75	−5.0	12.6	4.9		+7.7
9. C. W.	80.0	44.0	55	−5.5	12.6	5.9		+6.7
10. H. C.	75.0	48.1	64	−3.5	12.6	6.6		+6.0
11. N. F.	73.6	44.2	59	−8.7	12.6		8.3	+4.3
12. B. G.	72.7	54.4	75	−6.7	12.6		7.7	+4.9
13. C. W.	69.1	44.2	64	−4.7	12.6		4.8	+7.8
Mean			65.4		12.6	7.2	6.9	+5.5
Range			55-78			4.5-11.1	4.8-8.3	+1.5-+8.1
Standard deviation			6.8			2.2	1.5	2.0

alone were −9.0 Gm., −7.7 Gm., and −5.0 Gm., which were little different from the control losses in the depleted state, which were −8.7 Gm., −6.7 Gm., and −4.7 Gm., respectively.

DISCUSSION

The findings herein described establish the ability of the severely malnourished patient to retain for synthesis a high percentage of infused amino acid mixture given with a low caloric intake, both received intravenously. Following partial repletion, the nitrogen utilization was reduced on the same intake to the extent that in two of three patients a positive was replaced by a negative balance, and in the other the positive balance was greatly reduced. Even so, nitrogen was still utilized for synthesis, as shown by comparing the nitrogen balance during the administration of this mixture with that during the administration of an isocaloric intake consisting of carbohydrate alone.

These findings confirm observations in animals by Cox, Ellingson, and Mueller,[7] who found that protein-depleted rats and growing rats whose growth had been arrested for two weeks by starvation could continue to fabricate tissue protein, although at a submaximal rate, when the intakes were 36 per cent and 45 per cent of the optimal diet, whereas well-nourished adult rats lost body protein when their diets were restricted to less than 62 per cent of the optimal diet. Allison[5] showed that protein-depleted dogs fed a low-caloric diet went into positive nitrogen balance, the degree of which rapidly diminished as body-nitrogen stores increased until the twentieth day, when nitrogen

balance became negative. By contrast, well-nourished dogs, when fed the same ration, became less negative as depletion developed until the twentieth day.

TABLE II. DIFFERENCE IN NITROGEN BALANCE DURING INTRAVENOUS INFUSION OF GLUCOSE AND AMINO ACIDS BEFORE AND AFTER REPLETION

PATIENT	BODY WEIGHT IN PER CENT OF "NORMAL"	AVERAGE DAILY NITROGEN BALANCE		DAILY NITROGEN LOSS OF CARBOHYDRATE ALONE		PARTIAL REPLETION	
		BEFORE REPLETION (TABLE I) (GM.)	AFTER PARTIAL REPLETION (GM.)	BEFORE REPLETION (TABLE I) (GM.)	AFTER REPLETION (GM.)	DAYS	WEIGHT GAIN (KG.)
2. G. S.	85	+2.1	−3.3	−9.0	−8.7	15	3.6
7. N. Y.	64	+1.5	−2.3	−7.7	−6.7	15	9.1
8. N. B.	75	+7.7	+1.7	−5.0	−4.7	29	6.4

Confirmation also comes from the observation of Keys and his co-workers[9] on human volunteers. Although they stated that no correlation existed between nitrogen balances on the twelfth and the twenty-third days of semi-starvation, "the relative intakes of the different individuals were not precisely the same at the two periods." However, perusal of the data (Tables 192 and 193, page 383) reveals the interesting facts that three persons, Cases 119, 106, and 130, were actually given almost identical nitrogen and total caloric intakes during these two periods. In these three cases, the nitrogen balances on the twelfth day were −1.3, −3.4, and −1.8 Gm., respectively; on the twenty-third day −0.4, −2.3, and +1.7 Gm., respectively. It is thus seen that less nitrogen was lost as depletion advanced, confirming in a reverse way the findings herein presented.

Contrasting findings were reported by Ellison and associates[8] who studied nitrogen balance during the parenteral administration of a mixture of amino acids and glucose in two patients who had lost 15 to 20 per cent of their body weights. When the amount of nitrogen given remained constant at approximately 15 Gm. daily, and the glucose was increased in consecutive periods from 600 to 1,200 and to 1,800 calories daily, the nitrogen balance was found to become progressively more positive as the carbohydrate calories increased. The differences between these findings and those presented herein are probably due to differences in the state of nutrition of the patients studied (15 and 20 per cent loss of body weight as compared with an average of 35 per cent, respectively).

Although the caloric intakes in the present experiments were low, the question may well be raised as to whether they were inadequate in view of the reduced caloric needs of the malnourished person. To answer this question, body surface data would help, but unfortunately the heights of these patients are unknown, so that this figure cannot be used. However, in ten of the thirteen patients studied, only 400 nonprotein calories were given during the period in which amino acids were also administered. These 400 calories represent a 75 per cent reduction in the 1,600 usually considered as a minimum need for the normal adult at rest in bed. Now the average depleted weights in

these patients were 35 per cent below their normal. This represents severe inanition comparable to Benedict's "starving man," whose 29 per cent reduction in caloric needs was greater than the 20 per cent reduction in body weight. Thus it seems unlikely in the present undernourished patients that the need would be reduced by 75 per cent below normal, limiting consideration of intake to 400 glucose calories. This, of course, does not take into account protein intake as amino acids, which theoretically add another 400 calories, bringing the total to 800 or about 50 per cent of normal. However, this addition seems unjustified, as shown by the fact that the average nitrogen loss during the control period on glucose alone was 6.6 Gm., and during the amino acid period it was 7.1 Gm. Thus only 0.5 Gm., of the 12.6 Gm. given were used as calories, the rest being used to synthesize the protein. Since synthesis uses rather than yields calories, it seems clear that during the period of amino acid-glucose administration in these observations, the caloric needs would actually have been increased rather than decreased by the addition of amino acids.

The similarity in the nitrogen balance findings in the three patients receiving twice as much, or 800 nonprotein calories, was at first surprising and suggested that 400 is really not subcaloric for, if this were so, improved nitrogen balance might have been expected with a larger carbohydrate intake. On the other hand, it is hard to see how any better nitrogen balance could have been achieved, since such a high percentage of the infused amino acids was already being utilized for synthesis. A much more likely explanation of the present findings is one which refers to the state of protein stores. That this is more important than the caloric needs is indicated by the data on the three partially repleted patients in whom the amount of nitrogen retained for synthesis was reduced. This difference was probably due to restoration of tissue protein and not to any change in caloric needs.

The similarity in the loss of nitrogen on glucose alone during the depleted and the partly repleted state is of special interest in view of the findings of Johnson, Deuel and co-workers,[11] who found that the nitrogen-sparing effect of a nonprotein diet was directly proportional to the caloric intake. However, this was true only during the latter part of a ten-day observation period. From this it may be inferred that in the present experiments much less nitrogen would have been lost during the control days on glucose alone had a larger amount been given. Data reported by Ellison and associates[8] are somewhat at variance with the findings of Johnson and Deuel[11] in that the former found that the nitrogen lost on the fifth, sixth, and seventh days of a low protein intake averaged 6 Gm. per day in one case, and 7 Gm. per day in another case, despite a daily intake of 27 and 30 calories per kilogram. Similar losses were found in the present experiments on caloric intakes of 7 to 14 per kilogram. It is clear that further studies are needed to determine the most appropriate caloric intake which will achieve the maximum nitrogen sparing.

The present findings suggest, finally, that if the degree of positive nitrogen balance observed herein on a low caloric intake really measures the de-

gree of protein depletion, similar observations may be used as a quantitative method for determining the state of the tissue-protein stores. This possibility will be investigated in experiments which are now in progress.

SUMMARY

1. Strongly positive nitrogen balances have been consistently achieved in thirteen patients suffering severe inanition on a low caloric parenteral intake containing 100 Gm. of an amino acid mixture plus 400 or 800 carbohydrate calories as glucose. No difference was observed in the degree of nitrogen balance with this difference in caloric intake.

2. In three of these patients in whom the same infusion was repeated after partial repletion, the amount of nitrogen utilized for synthesis was greatly reduced.

3. It is inferred from these observations that the degree of nitrogen balance on a low caloric intake is related to the state of the protein stores and that this method may be used as a quantitative measure of the degree of tissue-protein depletion.

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CONTROL OF PAIN FOLLOWING HEMORRHOIDECTOMY

WALTER H. GERWIG, JR., M.D., SEYMOUR ALPERT, M.D.,
CHARLES S. COAKLEY, M.D., AND BRIAN BLADES, M.D.,
WASHINGTON, D. C.

(From the Departments of Surgery and Anesthesia, The George Washington University Hospital and School of Medicine)

PAIN following operations for hemorrhoids continues to be very distressing to many patients. The anticipation of discomfort is frequently augmented by the ever willingness of the patient's acquaintances to discuss freely, and maybe somewhat tactlessly, their own "ordeals" and "horrible experiences" following hemorrhoidectomy. It is understandable that patients about to undergo such an operation are often in a state of anxiety and apprehension, and such an attitude is certainly not one to be desired.

Blades and Ford[1] developed the technique of polyethylene-tube implantation near the intercostal nerves, and by intermittent injections of local anesthetic agents they created nerve blocks that abolished pain following operations on the chest. They suggested that their method might be of value in abdominal surgery. Gerwig, Thompson, and Blades[2] reported the use of this technique as employed in surgery of the upper abdomen as an aid in the reduction of the anticipated frequency of pulmonary complications.

This study was begun to determine if patients undergoing hemorrhoidectomy could be managed during the postoperative period in such a way so that pain could be abolished. Since many of the operations for hemorrhoids were being performed under transsacral and caudal anesthesia, it was speculated that by implanting a small plastic tube into the caudal canal, through which an anesthetic agent could periodically be delivered, pain might be abolished. The effect of these intermittent injections has been studied in fifty-nine patients undergoing hemorrhoidectomy with encouraging results.

The method employed was modified occasionally during the study until the best features could be incorporated. The technique consists of placing the patient in a prone jackknife position; the sacral area is carefully cleansed and draped; and a skin wheal of 1 per cent Novocain solution is made over the sacral hiatus using a 26 gauge, 5/8 inch needle. Through the anesthetized area a special 18 gauge, 2½ inch thin-walled caudal needle is inserted into the caudal canal. After making certain that the dura has not been penetrated, and that the tip of the needle is not in a blood vessel, 30 c.c. of 0.15 per cent Pontocaine Hydrochloride Solution is injected. A 60 cm. piece of vinyl tube, the lumen of which will admit a 23 gauge needle, is inserted into the caudal needle for two and one-half inches. The vinyl tubing is best sterilized by being autoclaved in a long glass tube and kept straight by a stylet. After the

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vinyl tube is placed, the caudal needle is then withdrawn over the tube. A blunt 23 gauge needle is inserted into the distal lumen of the plastic tube and a hub adapter applied. If necessary, additional anesthetic agency may be injected through the tube, or transsacral injections may be carried out. Dressings are applied to the sacral area and, by means of a long wide strip of adhesive tape, the plastic tube is secured to the skin and brought around the side of the patient to the front to facilitate later injections.

After the operation has been completed the patient is returned to bed and instructed to notify the charge nurse at the first signs of discomfort in the anal region. Usually this occurs after two to four hours. Using a different sterilized 20 c.c. syringe each time, the hub adapter is removed and 20 c.c. of 0.15 per cent Pontocaine Hydrochloride Solution is injected via the tube into the caudal canal. Prior to each injection, the patient is strongly encouraged to void. It is felt that this has kept bladder catheterization to a minimum. Usually it is not necessary to inject more often than every three hours and some patients do not need an injection for six or seven hours. The plastic tube is left in place during the first forty-eight hours postoperatively and then removed. The forty-eight hour period of pain abolition seems to avoid any conditioning or summation on the part of the patient, and confidence that there will be no pain is established. After the time of tube removal, the control of any minor discomfort is no problem.

An additional method of establishing a serene mental attitude for the patient is to inject some anesthetic solution the morning following operation and after a few minutes a digital examination is performed which will further convince the patient that pain can be completely controlled.

Neither antibiotics nor chemotherapeutic agents were employed in this series, and there has been no instance of infection associated with this tube technique in any of the fifty-nine patients. No circulatory disturbances, such as reduced blood pressure, were noticed. Urinary retention was not increased. The need for narcotics was sharply decreased, but all patients received barbiturates at night to aid them in sleeping.

The only contraindications to the employment of this technique appear to be those in which the use of caudal anesthetic is inadvisable.

SUMMARY

The results of this study indicate that the above technique is an easy, efficient, and safe method to abolish pain completely following hemorrhoidectomy. Additional studies are in progress at this time in order to further evaluate the efficacy of the procedure and to determine its usefulness in all types of anal surgery.

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LEIOMYOSARCOMA OF THE SMALL INTESTINE

CHARLES B. RIPSTEIN, M.D., AND GEORGE W. FLINT, M.D., BROOKLYN, N. Y.

(From the Department of Surgery, Maimonides Hospital of Brooklyn, and the State University of New York, College of Medicine at New York)

LEIOMYOSARCOMA of the small bowel is a relatively rare tumor, approximately seventy cases having been described in the literature.[3, 5] Of these, twenty were in the duodenum and fifty in the jejunum and ileum. In recent years, increasing numbers of these tumors have been reported and there is evidence to indicate an actual increase in their incidence. At Maimonides Hospital we have had the opportunity of treating nine cases of leiomyosarcoma of the small bowel. Of these, three were in the duodenum, two in the jejunum, and four in the ileum.

The duodenal lesions exhibit a characteristic clinical picture which closely mimics duodenal ulcer. Massive hemorrhage is a common complication.[6] The smooth muscle tumors of the stomach and duodenum have been discussed elsewhere[10] and this paper deals with lesions in the mobile part of the small intestine, the jejunum and ileum.

Pathology.—These tumors arise from the smooth muscle of the intestinal wall and they are composed of interlacing bundles of spindle-shaped cells with large vesicular nuclei and an abundant fibrillar stroma. Multinucleated cells may be present. The tumors are not encapsulated but tend to interdigitate with normal muscle at the periphery. They may grow inward forming polypoid masses in the intestinal lumen or outward as extrinsic masses. They are very vascular and exhibit a marked tendency to hemorrhage. Bleeding may occur into the bowel, into the peritoneal cavity, or into the tumor itself.

There has been a great deal of discussion as to the relative malignancy of smooth muscle tumors of the bowel.[5] Metastases are uncommon, being reported in 10 to 20 per cent of the cases.[8] Lymph nodes are rarely involved, most metastases being blood borne, with the liver as the common site. Lungs, bones, and brain may also be invaded. Histologically, the benign tumors do not differ from those that exhibit distant metastases and it is impossible to correlate cellular differentiation or mitoses with clinical behavior. The safest course is to regard all smooth muscle tumors of the gastrointestinal tract as potentially malignant. It must be emphasized, however, that they are of relatively low-grade malignancy and in the absence of distant metastases the prognosis is excellent following adequate surgical excision.

Clinical Features.—The clinical manifestations of these tumors fall into two groups, those due to bleeding and those due to the presence of a mass obstructing the bowel. The following case histories are illustrative.

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CASE 1.—A 49-year-old man was first admitted to Maimonides Hospital in 1941 complaining of intermittent tarry stools accompanied by attacks of syncope. These symptoms had been present for two years. Investigation, including barium series, was negative and the patient was discharged on an ulcer diet.

He was readmitted in 1942 and again in 1943 with the same complaints. On the third x-ray examination a circumscribed defect was noted in a proximal loop of jejunum. At laparotomy a walnut-sized tumor was found arising from the jejunum eight inches from the ligament of Treitz. Six inches of bowel including the lesion were resected and the patient made an uneventful recovery. Pathologic examination revealed a leiomyosarcoma of the jejunum. The patient has remained well and free from symptoms.

CASE 2.—A 44-year-old woman was admitted in January, 1951, with a one-year history of weakness, dizziness, epigastric distress, and tarry stools. Repeated gastrointestinal barium series, including small bowel studies, had revealed no pathology. She was treated for peptic ulcer but the tarry stools continued and the hemoglobin dropped to 48 per cent. At exploration there was a 3.0 cm. nodule on the antimesenteric border of the midileum with large veins on its surface. Resection and end-to-end anastomosis were performed and the patient made an uneventful recovery. The pathologic diagnosis was leiomyosarcoma.

CASE 3.—A 56-year-old man was admitted in April, 1951, with a seven-year history of recurrent episodes of tarry stools and weakness. Repeated barium studies of the gastrointestinal tract had failed to reveal any pathology. At laparotomy a 4.0 cm. mass was found arising from the antimesenteric border of the upper jejunum. Following resection and end-to-end anastomosis the patient made an uneventful recovery and has remained well.

Comment.—These three cases show a characteristic pattern of recurrent episodes of gastrointestinal hemorrhage for which no cause could be found on repeated radiologic examination. This emphasizes the need for surgical exploration in such cases. Despite the long duration of symptoms, no metastases were found at operation and the lesion was resectable in every instance.

CASE 4.—A 54-year-old woman was admitted to Maimonides Hospital because of the sudden onset of severe lower abdominal pain. There was a history of several episodes of tarry stools over a two-year period and a diagnosis of peptic ulcer had been made by the referring physician. The findings on admission indicated a lower abdominal peritonitis. The preoperative diagnosis was ruptured ectopic pregnancy and at exploration a considerable amount of free blood was found in the peritoneal cavity. This was coming from a necrotic mass 10 cm. in diameter arising from the distal ileum. Local excision of the mass was performed without resecting the adjacent bowel. Because of the pathologic diagnosis of leiomyosarcoma and the limited resection which had been performed the patient was re-explored three weeks later and an eight-inch segment of bowel was resected. Pathologic examination revealed residual tumor tissue at the site of the initial resection. The patient has remained well for over three years.

CASE 5.—A 38-year-old woman was admitted with a three-month history of intermittent midabdominal pain which suddenly became very severe. The preoperative diagnosis was acute appendicitis. At operation a considerable amount of blood was found in the peritoneal cavity, coming from a nodular mass on the antimesenteric border of the ileum. The tumor was excised and proved to be a leiomyosarcoma. The patient made an uneventful recovery.

Comment.—In these cases, intraperitoneal bleeding produced the clinical picture of an acute abdominal emergency. In Case 4, the hemorrhage was

so severe that a preoperative diagnosis of ruptured tubal pregnancy was made. This case emphasizes the necessity for adequate resection of the lesion. Re-exploration following local excision revealed residual tumor in the bowel wall.

CASE 6.—A 69-year-old woman was admitted to Maimonides Hospital, Oct. 23, 1951, with complaints of epigastric pain, nausea, and vomiting of three days' duration. She had had recurrent episodes of a similar nature for one year prior to admission. Physical

Fig. 1 (Case 6).—Barium x-ray picture showing a filling defect in the terminal ileum.

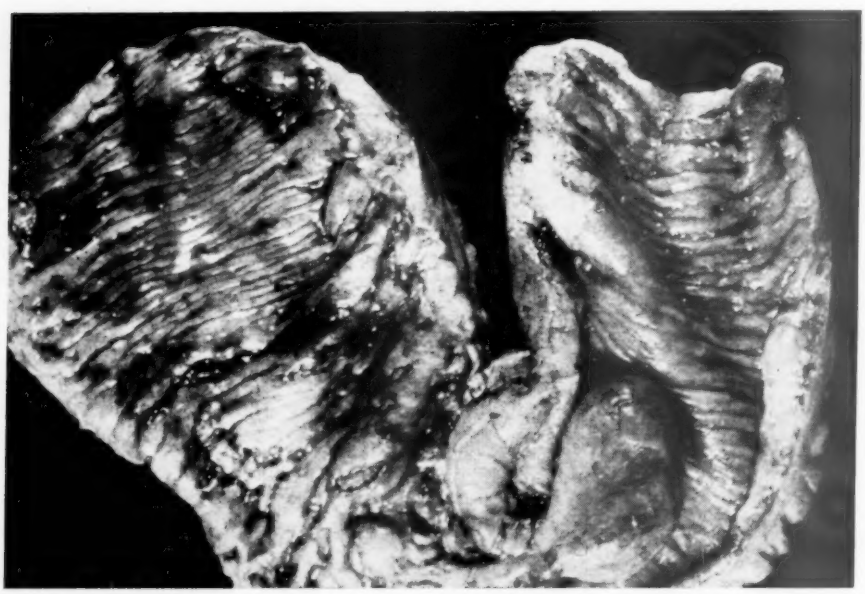

Fig. 2 (Case 6).—Intussuscepting leiomyosarcoma of the ileum.

examination revealed moderate abdominal distention and flat plate of the abdomen showed evidence of a mechanical small bowel obstruction in the region of the terminal ileum. Barium enema demonstrated an intussuscepting lesion in the terminal ileum and at laparotomy, this diagnosis was confirmed. The intussuscipiens was a smooth pedunculated tumor which proved to be a leiomyosarcoma. The involved bowel was resected and the patient made an uneventful recovery.

Comment.—In this case, the clinical picture of small bowel obstruction was produced by an intraluminal tumor mass leading to intussusception.

SUMMARY

1. Leiomyosarcoma of the small bowel is a relatively uncommon tumor but the incidence appears to be increasing.

2. These tumors are of low-grade malignancy and metastases are infrequent. However, it is impossible to predict the behavior of the tumor from its histologic appearance and adequate surgical resection is necessary in all cases.

3. The clinical manifestations are chiefly due to bleeding, either into the bowel or into the peritoneal cavity. In the former case, the picture is that of recurrent intestinal hemorrhage, and in the latter, that of an acute intraperitoneal emergency. Occasional cases present with episodes of acute intestinal obstruction.

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USE OF THE ROUX-EN-Y ILEAL URETERAL ANASTOMOSIS FOR REIMPLANTATION OF BILATERAL CUTANEOUS URETEROSTOMIES TO AN ILEAL POUCH

FRANK J. RACK, M.D., FIORINDO SIMEONE, M.D., AND HARRY TRATTNER, M.D.,
CLEVELAND, OHIO

(From the Departments of General Surgery and Urology, School of Medicine, Western Reserve University and City Hospital)

USE of an isolated segment of ileum with implanted ureters as a substitute bladder pouch draining into an ileostomy bag provides, under certain circumstances, satisfactory disposition of the ureters following total cystectomy.[1] It is the purpose of this report to describe an experience with massive hemorrhage from this type of pouch which required emergency transplantation of the ureters to the skin, resection of the pouch, and a new method for subsequent reimplantation of the resultant shortened ureters from the skin to a second ileal pouch.

CASE REPORT

C. B., a 70-year-old white man, was admitted to City Hospital on Jan. 1, 1952, because of dysuria of five months' duration. A diagnosis of squamous-cell carcinoma of the bladder was established by biopsy. Because of the complete absence of rectal sphincter tone transplantation of the ureters to an ileal pouch instead of ureterocolic anastomosis was considered the procedure of choice. On Feb. 19 a segment of low ileum was isolated from its course and intestinal continuity was re-established by ileoileal end-to-end anastomosis excluding the selected segment. One end of the isolated segment was closed and both ureters were implanted into it over polyethylene catheters; the other end of the segment was brought out through a stab wound in the right lower quadrant of the abdomen. Total cystectomy and prostatectomy were then completed. Shortly after operation a Foley bag catheter was inserted into the ileal pouch below the level of the abdominal wall and inflated to provide closed urinary drainage. The polyethylene tubes were removed at that time.

The patient made an uneventful convalescence and the catheter effectively drained urine for the next eighteen days. At that time, however, intermittent massive bleeding started from the ileal pouch. During the subsequent three days all attempts to stop the bleeding proved of no avail. Twenty-four units of whole blood were required to combat shock. On March 11, emergency operation was performed and both ureters were transplanted from the ileal pouch to the skin and the ileal pouch was excised completely. Pathologic examination of the ileal pouch revealed focal acute and chronic enteritis with ulceration. It was presumed that this represented reaction to the prolonged presence of the inflated Foley bag catheter. Postoperatively the cutaneous ureterostomies functioned well although there was slight dilatation at the upper urinary tract (Fig. 1). On May 1, 1952, the patient was reoperated upon through an upper abdominal transverse incision. Both cutaneous ureterostomies were dissected free and mobilized. The ureters were dissected back until normal tissue was reached. These ureteral remnants measured about 7 centi-

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meters. Another segment of ileum measuring about 30 cm. was isolated and intestinal continuity was re-established with ileoileal end-to-end anastomosis. The isolated segment was then again divided into two segments, one measuring about 10 cm., the other 20 centimeters. A Roux-en-Y type of anastomosis was then made between the two segments in such a way as to provide three limbs, each measuring about 10 cm. in length. The cephalad ends of the two limbs of the Y were then closed and into each blind limb one ureter was anastomosed after the method of Cordonnier[2] with two rows of sutures. The distal single limb of the Y was brought out through a stab wound in the left side of the abdomen as in the creation of an ileostomy and the wound was closed (Fig. 2). The patient made an uneventful recovery. Urinary drainage into an ileostomy bag started shortly after operation and has continued satisfactorily to date (Figs. 3 and 4).

Fig. 1.—Intravenous pyelogram, made during period patient had bilateral cutaneous ureterostomies, showing some dilatation of upper urinary tract.

DISCUSSION

This case demonstrates the danger of prolonged pressure on ileal mucosa. The use of the inflated Foley bag catheter seemed, at first sight, a more simple method of draining the ileal pouch than did the use of an ileostomy bag. It proved effective for eighteen days. Once hemorrhage started, however, all attempts to pack the pouch with gauze and Oxycel and to visualize the bleeding area with the cystoscope and sigmoidoscope failed. The patient lapsed repeatedly into shock as bleeding continued intermittently in spite of twenty-four transfusions. The need for delicate manipulation of the ileum and for avoidance of mucosal pressure, even in the absence of the fecal stream, is evident.

Emergency transplantation of ureters to the skin is often a lifesaving procedure as demonstrated in this patient. Although this type of urinary drainage is undesirable as a permanent measure it may be invaluable as a temporary expedient, for example, when dilated ureters are encountered during pelvic evisceration preventing immediate ureterocolic anastomosis or when after extensive surgery the patient's condition does not allow the prolongation of the procedure required to complete a careful ureterocolic or ureteroileal anastomosis.

As Beisler[3] stated, the adage that once a skin ureterostomy, always a skin ureterostomy, is no longer tenable. The literature is very meager on the reimplantation of skin ureterostomies into the bowel, and no reports are available concerning reimplantation into an ileal pouch.

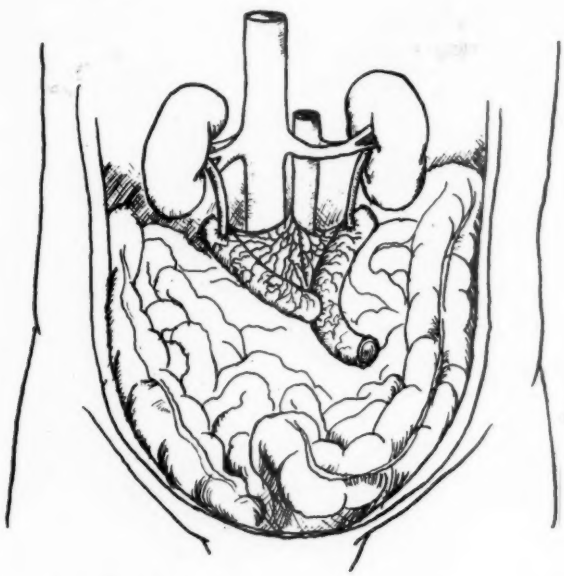

Fig. 2.—Drawing illustrating creation of ileal pouch utilizing Roux-en-Y principle and ureteral-ileal anastomoses.

One of the technical factors encountered in this case and often of concern in other similar cases of ureteral reimplantation is the fact that ureters that have been previously divided and exteriorized are found very much foreshortened when mobilized from the abdominal wall and dissected to normal tissue. This prevents satisfactory anastomosis without tension to the colon or to a simple ileal pouch. In this case if a simple ileal pouch had been employed during reimplantation, a long segment of ileum with a tense mesentery would have been required to bridge across from just below one kidney pelvis to just below the other pelvis and then through the abdominal wall for the external stoma. Use of the Roux-en-Y ileal arrangement provided for the use of a shorter segment of ileum, more direct and shorter drainage from each kidney, and ureteroileal anastomoses bilaterally without tension.

Fig. 3.—Postoperative photograph illustrating projection of ileal segment above abdominal wall to insure satisfactory function of urinary receptacle.

Fig. 4.—Intravenous pyelogram made after transposition of ureters from skin to ileal pouch showing normal upper urinary tract.

SUMMARY

1. A case report is presented wherein pressure from an inflated Foley bag catheter on the mucosa of an ileal pouch created as a bladder substitute caused massive hemorrhage requiring emergency transplantation of the ureters from the ileal pouch to the skin and excision of the pouch.

2. The subsequent reimplantation of the bilateral cutaneous ureterostomies to a second ileal pouch utilizing the Roux-en-Y principle to provide more direct and shorter drainage from each kidney and ureteroileal anastomoses bilaterally without tension is described.

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Case Reports

NONSPECIFIC GRANULOMATOUS INFLAMMATION (CROHN'S DISEASE) OF THE APPENDIX

A Case Report

Major Eugene V. Meyerding, Medical Corps, United States Air Force, Biloxi, Miss., and Lieutenant Colonel Harold F. Bertram, Medical Corps, United States Army, Fort Campbell, Ky.

(From Tripler Army Hospital, Honolulu, T. H.)

OUR knowledge of the entity, regional enteritis, has greatly expanded since Crohn, Ginzburg, and Oppenheimer[1] first described it twenty years ago. Hadfield[2] later described the histologic lesion, which is pathognomonic, thus distinguishing this disease from the other infectious granulomas. His work has been confirmed. The sites of involvement have been expanded, and now, according to Comfort and associates,[3] the disease is encountered anywhere in the gastrointestinal tract, from the stomach to the right colon, inclusive. Rarely is the appendix mentioned as being involved and, if so, it is mentioned only secondarily to involvement of the cecum or terminal ileum. We have been unable to find any mention of the appendix as the primary and sole site of involvement. Rappaport and his co-workers[4] studied 100 selected cases of regional enterocolitis. Their material was obtained from either surgical or necropsy specimens. In this series, adequate material was available for study of the appendix in only thirty-five instances. Of these thirty-five, they found a granulomatous process present in twelve cases. Seven of these twelve had typical nodular granulomas. Rappaport does not state whether the appendices were involved alone or with the ileum and/or cecum. We cannot make inferences from his study.

In 1937 Ravdin and Rhoads[5] described what they called fibroplastic appendicitis. They discussed the similarity between this condition and regional enteritis. They pointed out two differences which, we believe, establish these diseases as distinct and separate entities. These differences are that mucosal ulceration is prominent in regional ileitis and much less marked in fibroplastic appendicitis, and that giant cells were frequent in the sections studied from their cases of regional ileitis and were not observed in fibroplastic appendicitis.

We wish to record a case of appendical inflammation in which the microscopic lesions are identical with the lesions of regional enteritis, but in which the ileum and cecum are grossly normal.

CASE REPORT

A 21-year-old white man was admitted to Tripler Army Hospital on Aug. 23, 1951. He stated that he was well until about noon of the day of admission. Shortly after a

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noon meal of pork, dressing, and pie he experienced sharp, cramping epigastric pain and continuous pain in the right upper quadrant of the abdomen. He was not nauseated and did not vomit. He had had a normal bowel movement the morning of admission. There were no symptoms referable to the urologic tract. There was no significant history of diarrhea in the past. He had noticed anorexia associated with "indigestion" on several occasions during the three months prior to admission. He denied any weight loss. He remembered one previous attack of severe epigastric pain, several months before the present illness, which lasted only a few hours and subsided without treatment. Past personal and family histories were noncontributory. He had been in the Central Pacific area since March, 1949, but, with this exception, had not been ill since arriving in that area. He was admitted to the hospital two hours after onset of symptoms.

Fig. 1.—Low-power view showing marked thickening of appendical wall, mucosal ulceration, and the large distorted lymphoid follicles.

Physical Examination.—The patient was in obvious distress because of acute abdominal pain. He was five feet, seven inches tall and weighed 160 pounds. Admission temperature was 102.8° orally, blood pressure was 155/85, pulse rate was 100 per minute, and respirations were 18 per minute. The heart and lungs were within normal limits. There was exquisite tenderness to palpation throughout the abdomen, with maximum tenderness as well as pain in the right upper quadrant. Muscle-guarding was marked over the entire abdomen. Rebound tenderness was present in both lower quadrants. No masses could be felt. Re-examination of the abdomen one hour later revealed pain reference to the right periumbilical region and the right lumbar area. No costovertebral angle tenderness could be elicited. Marked psoas muscle irritation was demonstrable. Rectal examination revealed tenderness throughout the pelvic area. The remainder of the physical examination was not remarkable.

Laboratory Findings.—White blood cell count was 15,200 with 77 per cent neutrophils, 21 per cent lymphocytes, and 2 per cent monocytes. Red blood cell count was 4.3 to 5.3 million with 15 Gm. hemoglobin and hematocrit of 46. Urinalysis was within normal limits. Serum amylase determination showed 10 per cent starch hydrolysis (up to 35 per cent is considered normal). Roentgenograms of the chest and abdomen revealed nothing remarkable. The serology was negative.

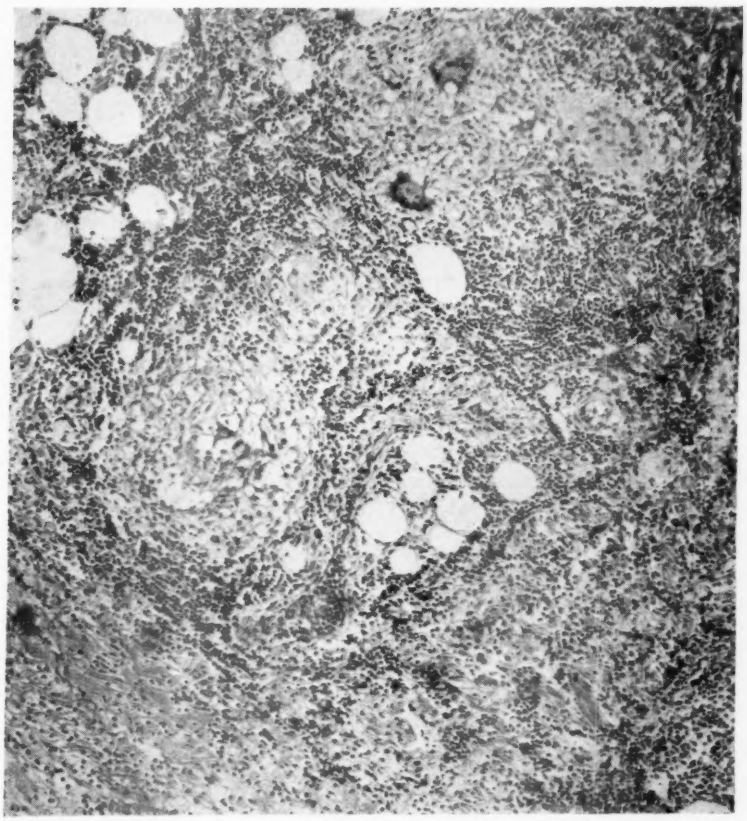

Fig. 2.—High-power view showing marked inflammatory infiltrate, tuberculoid formation, giant cells, and epithelioid cells. (Note absence of caseation.)

Course in Hospital.—Eight and one-half hours after onset of the symptoms, the patient was operated upon under subarachnoid Pontocaine anesthesia through a lower right rectus incision. A moderate amount of seropurulent fluid was seen as soon as the peritoneum was opened. The appendix was situated posterior to the cecum. The appendix was removed and, grossly, was markedly swollen, greenish black in color, and covered with a purulent exudate. The cecum and terminal ileum were normal in thickness and texture, although there was moderate hyperemia of the surfaces which were adjacent to the appendix. The operating surgeon has been interested in enterocolitis for several years and believes that, if any gross evidence of this disease had been present in the cecum or terminal small bowel, he would have recognized it. Because of the obvious purulent nature of the peritoneal fluid, the abdomen was not explored further. One gram of streptomycin and 1,000,000 units of penicillin were instilled in the peritoneal cavity, a small rubber tissue Penrose drain was placed down to the appendical fossa, and the incision was closed. The patient's convalescence was complicated by abdominal distention on the second postoperative day and by a wound infection. The distention responded well to gastric suction and Prostigmine. The wound infection cleared on routine management. The patient received 300,000 units of penicillin and 0.5 Gm. of streptomycin twice daily during convalescence. He was afebrile after the fourth postopera-

tive day. Barium enema and upper gastrointestinal roentgenographic study with special attention being paid to the small bowel, both done three weeks after operation, were considered to be entirely within normal limits. The patient returned to full duty five weeks after the operation.

Pathology.—The formalin-fixed appendix measured 11 cm. in length and 3 cm. in diameter at its greatest diameter. The surface was covered by a fibrinous exudate showing areas of hemorrhage through the exudate. Microscopically, the appendical lumen was filled with purulent exudate. The mucosal glands and surface epithelium were completely lost. The lymphoid follicles were enlarged and distorted. The wall was greatly thickened by edema, inflammatory infiltration, hemorrhage, and early fibrous tissue and capillary proliferation. The infiltrate was composed of lymphocytes, eosinophils, plasma cells, segmented neutrophils, epithelioid cells, and multinucleated giant cells. There were many giant cells having an abundant pink-stained cytoplasm and multiple small oval nuclei. In most of the giant cells, the nuclei were distributed peripherally, but in some the distribution was irregular. The epithelioid cells occurred in groups, frequently associated with giant cells. These groups resembled tubercles, but in none was caseation necrosis seen, nor could acid-fast bacilli be demonstrated after repeated studies of several slides specially stained. Figs. 1 and 2 show low-power and high-power views of cross sections of the appendix.

Follow-up Studies.—The patient's gastrointestinal tract was again studied by barium meal and enema nine months after surgery, and no abnormalities could be found. Upon direct questioning, no history was found of association with an individual either known to have, or suspected to have, tuberculosis. Early in 1952 the patient was skin tested with purified protein derivative tuberculin, both first and second strengths, and both tests were negative. The patient was remained asymptomatic for one year following surgery.

SUMMARY

We have presented a case of chronic, nonspecific granuloma, identical with Crohn's disease, arising within the vermiform appendix and without demonstrable involvement of the adjacent gastrointestinal tract. The similarity between this condition and tuberculosis is recognized; however, we believe that the absence of tubercle bacilli after careful study, the negative skin tests, and the absence of history of exposure to or infection by tubercle bacilli justify our conclusion. We believe that only rarely is the appendix involved in Crohn's disease, and we know of no other case reported in which the appendix was the sole site of involvement.

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ANASTOMOSIS OF COMMON AND INTERNAL CAROTID ARTERIES FOLLOWING RESECTION OF DEFECTIVE PORTION

Report of a Case

Patrick C. Shea, Jr., M.D., and J. Harold Harrison, M.D.,* Atlanta, Ga.

(From the Whitehead Department of Surgery, Emory University, and the Grady Memorial Hospital)

THE prohibitive mortality rate following ligation of the internal carotid artery should stimulate efforts to re-establish its continuity whenever defects exist or are produced. Resection of a portion of the internal or common carotid artery may become necessary (A) in the treatment of carotid aneurysms or arteriovenous fistulas, (B) in repair of these vessels following trauma, (C) in excision of carotid body tumors, and (D) in neck dissections for metastatic carcinoma where the tumor is adherent to or invades the vessel.

A successful end-to-end anastomosis of the internal and common carotid arteries was recently effected after excision of 3.3 cm. of the carotid artery at the bulb (bifurcation of the internal and external carotid arteries). The artery was the site of moderate atherosclerosis, which frequently militates against successful anastomosis. For this reason, and because of the paucity of similar reports in the literature, this case and discussion are presented.

CASE REPORT

A 39-year-old Negro man was admitted to the surgical service of the Grady Memorial Hospital, on Oct. 30, 1951, for excision of a tumor of the right maxillary antrum. Data from the hospital record revealed that a mass had been present in this area since 1928. The patient stated that a "dental cyst was removed from the upper right jaw area in 1935" and that the right external carotid artery was ligated at that time. In 1938, the right jaw became infected and it was incised and drained.

The patient was well developed and well nourished, with a temperature of 98.6° F., pulse 80, respiration 20, and blood pressure 170/100. General physical, neurological, and laboratory findings were normal. Pertinent physical abnormalities were confined to the right side of the face, which was asymmetrical in the antral region of the maxilla, with a definite hard mass palpable in and under the subcutaneous tissue. This mass, which extended into the oral cavity, appeared clinically to replace the right antrum. The patient had experienced severe episodes of bleeding from the oral aspect of the tumor, especially from sites of recent biopsies.

Because of the recurrent, exsanguinating hemorrhages, the patient was taken to the operating room on Nov. 6, 1951, for removal of the mass, although its true nature had not been established by the histologic examinations. Utilizing Pentothal Sodium and gas-oxygen anesthesia with an endotracheal airway, the left external carotid artery was ligated, in accordance with the operator's custom, to reduce bleeding when the tumor was removed. The right external carotid artery had been ligated several years previously, and dissection was begun through the old scar to eliminate any arterial collaterals that had developed in the interim.

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*Assistant Resident in Surgery, Grady Memorial Hospital.

During dissection of the common carotid artery for proper identification of its branches, severe hemorrhage developed and was controlled in the depth of the wound by application of a large hemostat to what was believed to be a branch of the common or external carotid artery on the right. After the bleeding stopped, further exploration revealed that the hemostat had been applied across the carotid bulb. At this point in the procedure one of us (P. C. S.) was asked to see the patient in consultation.

The existing incision was extended almost vertically, parallel to the sternocleidomastoid muscle, and the carotid artery was exposed from the base of the skull to approximately two inches above the clavicle. Proximal exposure was increased by retraction. The carotid artery was isolated from its bed and from its fascial integrity with the jugular vein and vagus nerve by sharp and blunt dissection. Several small vessels in the operative area were ligated. The hemostat, which had been applied directly to the bulb, was seen to have fractured it.

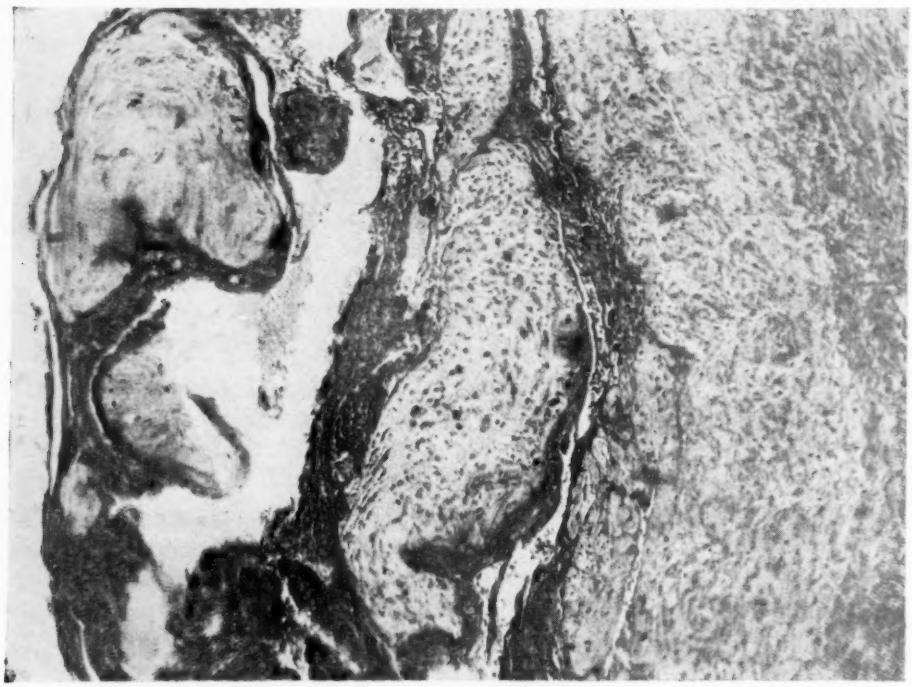

Fig. 1.—Photomicrograph of segment of common carotid artery, showing marked atherosclerosis. (Hematoxylin-phloxine stain.)

Blood flow in the internal carotid artery was controlled by finger pressure, the common carotid artery was obstructed by a Penrose rubber drain twisted and held under tension, and hemostat was removed. The condition of the artery was such that simple repair was impossible. Portions of atherosclerotic plaques (Fig. 1) could be lifted free from the vessel walls at the site of the created defect.

The patient's condition, already grave as a result of repeated hemorrhages, was intensified by this unforeseen situation. Tests to evaluate the patient's ability to tolerate cessation of cerebral circulation on one side had not been made prior to the operation; he was now completely anesthetized, and no such tests could be made. The additional factors of hypertension and arteriosclerosis indicated that he might not tolerate occlusion of the internal carotid artery. Preservation of cerebral circulation, if possible, appeared preferable to ligation of the damaged artery.

Since the external carotid artery had already been ligated, the damaged area at the bifurcation was resected, leaving a stump of the common carotid artery proximally and of the internal carotid artery distally. The vessel ends were débrided and fashioned for end-to-

end anastomosis. As the needle bearing the arterial suture was applied and purchase was obtained, a ring of atherosclerotic material 1 mm. wide pulled away when tension was applied. Débridement of the ends of the internal and common carotid arteries was, therefore, continued until an apparently normal segment of the internal carotid artery was reached. The common carotid artery still appeared markedly sclerotic, and when débridement was completed a 3.3 cm. deficiency in length resulted (Fig. 2).

Three through-and-through guide sutures of No. 00000 arterial silk were used to approximate the two ends, and the remainder of the anastomosis was carried out with interrupted silk sutures, interposing several horizontal mattress sutures for intimal eversion. The segment of internal carotid artery remaining below the base of the skull after débridement was so short that the first assistant had to hold it closed with a Halsted mosquito hemostat, with its box lock open, while the anastomosis was carried out. The artery between the hemostat and Penrose drain was then filled with about 3 c.c. of normal saline solution containing 20 mg. of aqueous heparin, and all air was excluded from the lumen.

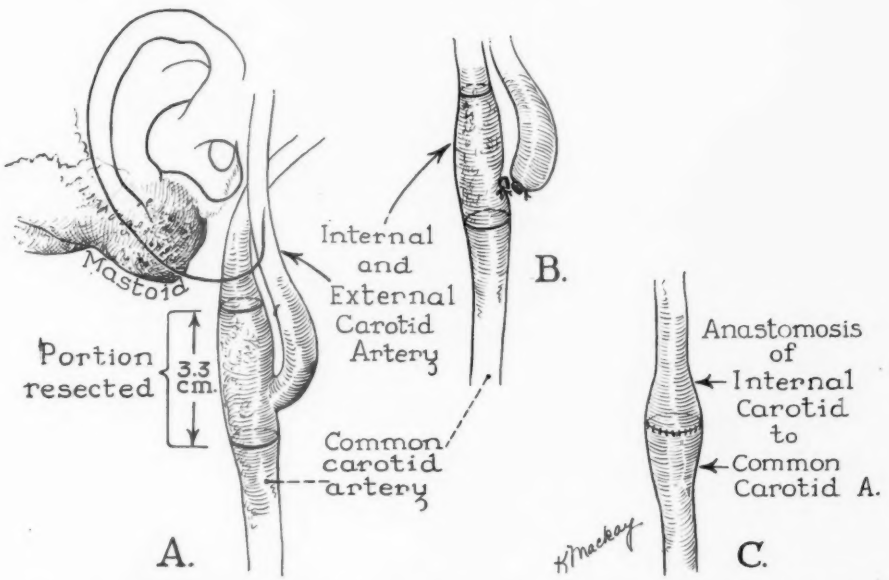

Fig. 2.—Diagrammatic drawing, showing *A*, portion of carotid artery resected, *B*, ligation of external carotid artery, and *C*, anastomosis of internal and common carotid arteries.

At the completion of the anastomosis, the Halsted hemostat was removed from the internal carotid artery and no bleeding occurred. When the rubber drain obstructing the proximal flow was removed, a temporary leakage from the anastomotic site was easily controlled by pressure until it ceased.

A periarterial sympathectomy, consisting of stripping the adventitia, was performed from one inch below the anastomosis to a level opposite the base of the skull. The area of anastomosis was wrapped with saline-moistened Gelfoam pledgets. The carotid pulse was full and bounding and there was no bleeding. The wound was closed in layers with sutures of silk,

Approximately sixty-five minutes had elapsed from the time the patient was first seen by us in the operating room until the anastomosis was complete.

Postoperative use of anticoagulants in this patient was not feasible because of the freely bleeding oral surface of the tumor. Two hours after the operation the patient reacted. His blood pressure was 180/140. He was restless and thrashed about and rolled his head. At this time a complete left hemiplegia existed. Three and one-half hours after the operation, slight motion in the left leg was induced by painful stimuli, the swallowing reflex returned, but no other resolution of the hemiplegia was observed.

The following day paresis was present in the left leg, but the left arm remained completely paralyzed. That evening, from the oral aspect of the tumor surface, the patient lost approximately 600 c.c. of blood, which was replaced by transfusion.

On the second postoperative day a tracheotomy was effected to facilitate treatment of a profuse bronchorrhea. The neurological status remained unchanged.

Three days following the anastomosis, another severe hemorrhage occurred, and the patient was again brought to the operating room and the entire antral tumor with its oral extension was removed. Grossly the tumor extended to—but not into—the dura. Pathologic study of the specimen later revealed a completely excised malignancy consistent with ameloblastoma.

Fig. 3.—Arteriogram of right common and internal carotid artery anastomosis, revealing patency. Slight dilatation at the site of anastomosis is result of only partial excision of the carotid bulb and of stripping of the adventitia in this area.

On the fourth day after anastomosis, the patient moved the left leg well and function returned in the left shoulder girdle muscles. The following day carotid pulsations were palpated for the first time—wound edema had previously precluded this observation. On November 16, ten days after arterial anastomosis, the patient's sensorium was clear and normal, and there was progressive improvement of motion in the left arm. On the thirteenth day the patient walked about the ward without difficulty; weakness of the left hand constituted the only neurological residual. A neurological examination on the twentieth day revealed normal balance except for loss of function in the intrinsic muscles of the hand.

On Nov. 30, 1951, twenty-four days after anastomosis, an open arteriogram, which was performed by exposing the right common carotid artery immediately above the clavicle and injecting Thorotrast (Fig. 3), revealed patency with slight dilatation at the site of the periarterial sympathectomy. The patient remained well and was last seen on April 14, 1952. The intrinsic muscle weakness of the left hand persisted at that time.

DISCUSSION

As early as 1857, Wood[1] stated that the consequences following complete and permanent obstruction of one of the two vessels supplying the brain with its greatest supply of blood render ligation of the common carotid artery a subject for grave consideration. Summers,[2] in 1897, recommended that an attempt be made to suture partially divided arteries in those cases where ligation might be followed by dangerous or perhaps fatal complication.

The severe mortality and morbidity which frequently follow interruption of carotid artery circulation,[3-7] especially that of the internal carotid artery, make restoration of cerebral circulation mandatory—unless cessation is necessary, as in the treatment of intracranial aneurysm. Even after resection of a portion of the common or internal carotid artery in the treatment of carotid body tumors, arteriovenous fistulas, or cancer of the head and neck, circulation can, in many instances, be re-established by end-to-end anastomosis, as demonstrated by several case reports.[8-11] These reports of common-to-common anastomoses are of interest because of variations in technical problems.

A review of the surgical literature of the past thirty-nine years reveals only one other report of anastomosis of the common and internal carotid arteries. Enderlen,[12] in his discussion "Surgery of Carotid Body Tumors" in 1938, cited an instance which had occurred twenty years previously with a woman patient in her middle sixties:

> . . . A carotid body tumor, originally considered as lymphoma, proved to be inseparable from the vessels. The bifurcation of the carotid was resected together with the tumor. The external carotid was ligated and the common carotid artery was anastomosed to the internal carotid artery by three traction sutures and a continuous circular suture with a straight arterial needle. The head was immobilized in a corresponding position by a cast. Recovery followed without any disturbance in the central nervous system. . . . Fourteen days later a carotid body tumor was excised from the opposite side of the neck without difficulty.

Two other successful cases of internal and common carotid artery anastomosis are known to the authors. In 1950, McDougall,[13] in an operative procedure for resection of invasive carcinoma in the neck, was forced to resect a portion of the common and internal carotid arteries and perform an end-to-end anastomosis. He reported: "A successful result was obtained and the patient survived the procedure but was lost to follow-up several weeks later."

Gage,[14] citing a case similar to Enderlen's, stated:

> . . . Dr. Champ Lyons dissected up the carotid arteries, removed the carotid body tumor, sacrificing part of the common carotid, and did an end-to-end suture of the common carotid to the internal carotid. The patient was given anticoagulants postoperatively and made an uneventful recovery and has remained well without cerebral sequelae.

Anastomosis of the common artery to the internal carotid artery may be somewhat difficult because of the limitations of exposure and operative space imposed by the base of the skull. Gage[14] pointed out the importance of dissecting up the common, external and internal carotid arteries through their entire length in order to accomplish a primary anastomosis between the common and internal carotid arteries. In amplifying this statement,[15] he added that severing the branches which fix the common carotid artery and external carotid artery and a few muscular branches from the internal carotid artery allows considerable longitudinal lengthening of the vessels. He further stresses the necessity of dividing the external carotid artery, as it fixes the vessels of the neck.

Although anticoagulants are not essential to patency following major vessel anastomoses,[9, 16] in the carotid artery—especially in cases with profound atherosclerosis—their use increases the probability of good results. No deaths occurred in Pemberton and Livermore's[4] four patients who were given anticoagulants after excision of a carotid body tumor and ligation of the internal carotid artery. In the case presented here, anticoagulants were contraindicated and a patent anastomosis was obtained without them.

In both this case and in Sloan's,[10] successful end-to-end anastomosis was accomplished even though it was necessary to place the sutures through markedly sclerotic vessels. Atherosclerosis, although an undesirable complication, is not inevitably a contraindication to adequate arterial reconstruction.

Re-anastomosis of the common and internal carotid arteries with relatively prompt restoration of cerebral circulation may have resolved this patient's hemiplegia. Recovery alone, without adverse neurological manifestations, is not proof that the carotid artery is patent after anastomosis, since survival without neurological changes can occur after ligation of the common or internal carotid artery. Nevertheless, neurological changes are progressive in many cases of interrupted carotid circulation and late cerebral complications may also increase progressively when the carotid artery, common or internal, is ligated.[5, 11]

Sooner or later in the experience of any surgeon doing head and neck surgery the need may arise to perform arterial anastomoses in the neck area following resection because of invasive carcinoma or, perhaps, trauma to sclerotic vessels. The procedure should certainly be included in the repertoire of the military surgeon.

SUMMARY

1. A successful case of end-to-end anastomosis of the right common and internal carotid arteries, following resection of a 3.3 cm. defective portion, is presented.

2. A photomicrograph demonstrates the amount of atherosclerosis present. A photograph of the arteriogram reveals patency after anastomosis.

3. A collected series of three similar cases is reported.

4. Re-establishment of carotid circulation should be considered when carotid body tumors, arteriovenous fistulas, or invasive carcinomas require partial excision of this vessel.

The authors are indebted to the Department of Pathology for preparation and description of the photomicrograph and to Dr. George Schimert, Assistant Resident in Surgery, for translation of references 1 and 7 from the German.

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Editorial

The Role of the Nervous System in the Pathogenesis of Duodenal Ulcer

THE concept that duodenal ulcer is in some way due to the tensions and strains of modern life has continued to interest physicians since Harvey Cushing[1] focused attention to this problem by his paper on peptic ulcer and the interbrain in 1932. Reference to duodenal ulcer as a psychosomatic disease or the wound stripe of civilization gives expression to this point of view. Many physicians have called attention to the high incidence of ulcers in persons whose occupations subject them to continuous mental strain, worry, and anxiety, and to the tendency for exacerbations to occur during periods of emotional stress. How can the tensions of modern life produce disturbances in the central nervous system which affect the stomach and produce a progressive, perforating ulcer? Several years ago I[2] postulated that these events cause a hypertonus in the secretory and motor fibers in the vagus nerves, resulting in hypermotility and in excessive continuous secretion of gastric juice in the empty stomach. That such a hypersecretion of gastric juice may be the primary cause of duodenal ulcer is indicated by the fact that a hypersecretion of similar degree in experimental animals regularly leads to peptic ulcer formation, and the abolition of this hypersecretion by complete gastric vagotomy in man causes the duodenal ulcer to heal.

Recently Gray and his associates[3] have suggested an alternate mechanism by means of which chronic stress may play an etiological role in duodenal ulcer. Thus it has been postulated that in response to emotional and systemic stress, the cells of the anterior hypothalamus secrete a humoral substance which stimulates the pituitary gland to release corticotropin. Corticotropin then increases the liberation of adrenal corticoids such as cortisone from the adrenal cortex, and these in turn stimulate the gastric glands to an increased production of pepsin and hydrochloric acid. This theory accounts for the hypersecretion of gastric juice in response to stress by a mechanism independent of the vagus-nerve supply to the stomach, and if valid would remove an important consideration for the employment of vagotomy in the treatment of duodenal ulcer.

When corticotropin and cortisone were first used as therapeutic agents there were conflicting reports in the literature of the effect of these drugs on peptic ulcers. Some investigators believed that corticotropin and cortisone had a beneficial effect on these lesions. Many recent observations have indicated, however, that both of these agents may produce an exacerbation of ulcer symptoms, even leading to perforation. Both corticotropin and cortisone have been found to produce a sustained and marked increase in the secretion of gastric juice in both man and experimental animals. In recent

experiments my associates, Zubiran, Kark, and Montalbetti,[4, 5] and I have found that this stimulation of secretion may be seen in dogs even after excision of the gastric antrum and removal of the vagus-nerve supply to the stomach. It is thus evident that the stimulating effect of these substances is exerted directly on the gastric glands and not on the nervous system or through the release of the gastric secretory hormone, gastrin.

Support for the hypothesis of Gray has been provided by a study by Porter, Movius, and French[6] which appeared recently in this JOURNAL. These investigators found that, in the monkey, stimulation of the anterior hypothalamus causes a secretion of gastric juice in the stomach which is prevented by vagotomy. A secretion of gastric juice may also be produced by stimulation of the posterior hypothalamus, and this stimulus seems to be conducted humorally through the pituitary-adrenal system. The response to this stimulation occurs later and is prevented by adrenalectomy but not by dividing the vagus nerves.

It remains to be demonstrated, however, that the tensions and strains encountered in the daily life of duodenal ulcer patients provide adequate stimulation for the hypothalamic-pituitary-adrenal axis. In a large series of duodenal ulcer patients studied in this clinic, in whom a profound hypersecretion of gastric juice in the fasting stomach was found before operation, this hypersecretion was reduced to approximately the normal level in 98 per cent of patients by a complete gastric vagotomy. If the hypersecretion were due to the adrenal stress mechanism we should expect that this hypersecretion would continue after vagotomy, since the stimulating effect of cortisone on the gastric glands persists even after both vagus denervation and extirpation of the antrum. The experiment appears to be a conclusive one, and suggests that in duodenal-ulcer patients the central nervous system plays an undoubted role increasing the secretion of gastric juice through excessive impulses over the vagus nerves and not the release of corticotropin with its secondary effect of augmenting the output of cortisone from the adrenal glands. However, the occurrence of peptic ulceration after severe burns (Curling's ulcer) and other serious traumas could be dependent upon this mechanism since there is better evidence that these severe bodily stresses excite the adrenal mechanism. Further investigation in this field will be awaited with great interest.

—*Lester R. Dragstedt.*

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE SURGICAL TREATMENT OF BREAST CANCER

AN HISTORICAL AND COLLECTIVE REVIEW

EDWARD F. LEWISON, M.D., BALTIMORE, MD.

(From the Breast Clinic Division of the Tumor Clinic, Johns Hopkins Hospital and Johns Hopkins University)

Let us not lightly cast aside things that belong to the past, for only with the past can we weave the fabric of the future.

Anatole France

THE epic of breast surgery is a pageant of time rich in the biography of many men of medical eminence. In the story of these skillful and courageous surgeons are prophecies of the past, the revelations of which have already cast their brilliance upon the present scene and give promise of adding luster to the triumphs of the future. The progress of science and surgery—microbiology and medicine—has been made possible by men whose aspirations and accomplishments have been far ahead of their time. In paying respect to these praiseworthy pioneers in their crusade against breast cancer our own modest efforts are lost in admiration. With deference and humility we give tribute to these venturesome spirits. As Sir William Osler reminds us "in the continual remembrance of a glorious past individuals and nations find their noblest inspiration."

For much of this historical material I acknowledge a great indebtedness to many sources, not the least of which are the learned and comprehensive essays of Sir D'Arcy Power of England and William A. Cooper of the United States.

The oldest historical records indicate that cancer was a dire disease of both animal and man in earliest antiquity. Preserved relics of prehistoric times—ancient bones and paleopathologic remnants—reveal a wide geographic and zoologic distribution of malignancy. Dinosaurs of the Mesozoic period are said to have shown signs of cancer, and other evidences of its antiquity (Sambon cited by Haddow) are to be found in the treasures of the pyramids, from the Etruscan tombs, from Peruvian mummies, and from the cuneiform tablets of the library of Nineveh. However, despite its world-wide dissemination, cancer appears to have been relatively uncommon in prehistoric times. Perhaps the limited survival of primitive peoples prevented them from attaining the so-called "cancer age." Sigerist in the first volume of his classic masterwork of medical history refers to the curious observation that cancer of the soft tissues (including the breast) has never been found in an Egyptian mummy. It must be remembered, however, that the total number of mummies which have been medically examined is probably relatively small.

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The earliest medical record known to modern man is the "Edwin Smith Surgical Papyrus." This relic of antiquity is regarded by historians as having been originally written in the Egyptian Pyramid Age in the Old Kingdom (3000 to 2500 B.C.). Although the manuscript gives no hint as to its author, an interesting speculation by Breasted and Cooper suggests that this document may very well represent in part the teachings of the oldest known physician,

Fig. 1.—Breast examination. From the Herbal of Pseudo-Apuleius (late thirteenth century), Bibloteca Medicea Laurenziana, Florence, Italy. Pult. 13, cod. 16, fol. 51 r. Translation: For pain in the breast of women who have milk or a tumor. Grind and mix herba proserpinaca (knotgrass) with butter and apply to dispel pain wondrously and cause the tumor to disappear. Translation from: E. Howald and H. E. Sigerist (Editors) Pseudoapulei Herbarius, Corpus Medicorum Latinorum, Vol. IV, p. 54. Leipzig and Berlin Teubner, 1927.

Imhotep, the patriarch and sage of primitive medicine who lived in the thirteenth century B.C. In the translation and commentary of this papyrus published by J. H. Breasted of the University of Chicago one finds a series of eight cases concerned with tumors or ulcers of the breast. The nature of the ailment is not always clear, but the available evidence indicates the disease to be breast tumors or possibly ulcers. Treatment by cauterization with the fire-

drill (Fig. 2) is the oldest known reference to this practice. In discussing bulging tumors of the breast, the following instructions are to be found in the "Edwin Smith Surgical Papyrus":

> If you examine a man having bulging tumors on his breast, and you find that they have spread over his breast; if you place your hand upon his breast tumors and you find them to be cool, there being no fever at all therein when your hand feels him; they have no granulations, contain no fluid, give rise to no liquid discharge, yet they feel protuberant to your touch, you should say concerning him: "This is a case of bulging tumors I have to contend with."

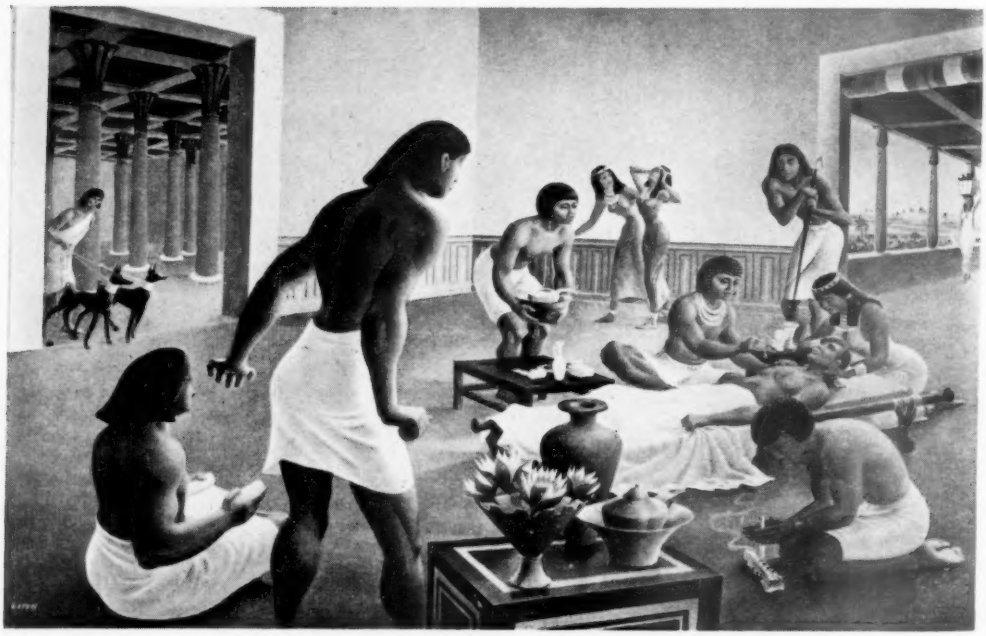


Fig. 2.—Artist's conception of treatment of breast disease by cauterization with the fire drill (courtesy of Lederle Laboratories).

The ancient Egyptian sage then goes on to say with simple honesty, "There is no treatment." A brief commentary then follows perhaps written by a more "modern" contemporary something less than five thousand years ago:

> Bulging tumors on the breast mean the existence of swellings on the breast, large, spreading and hard; touching them is like touching a ball of wrappings; or they may be compared to the unripe hemat-fruit, which is hard and cool to the touch like the swellings on the breast.

Thus, certain types of benign or malignant tumors of the breast appeared to be rather well differentiated from pyogenic mastitis and breast abscess discussed in a preceding part of the Edwin Smith Papyrus.

The Ebers Papyrus which dates from a later period (circa 1600 to 1500 B.C.) is a collection of cases, prescriptions, and incantations without any known reference to cancer of the breast. However, a fatty tumor is described which was successfully treated "with the knife." In treating an abscess the following recommendation is made: "When thou findest a purulent swelling with the

apex elevated, sharply defined and of a rounded form, then sayest thou, It is a purulent tumour which is growing in the flesh—I must treat the disease with the knife.'' Thus, the incomplete manuscripts of ancient Egypt indicate that simple fractures and dislocations were manipulated and splinted, abscesses were opened with the cautery and later the knife, tumors were cauterized and wound surgery consisted of coaptation of the skin edges. In reviewing primitive pre-Homeric Egyptian surgery there is no evidence to suggest that an operative procedure was used in the treatment of cancer of the breast.

In the history of Herodotus, a historian who lived just prior to Hippocrates, we are told that Atossa, daughter of Cyrus and wife of Darius, had a tumor of the breast which, after a time, ulcerated and spread. So long as it was small, from false modesty, she concealed it and told no one about it, but when it began to grow and give her trouble she sent for the famous physician Democedes (who lived in Greater Greece about 525 B.C.) and he cured her. However, no mention of his therapeutic method is made. Herodotus gives a detailed account of the prowess of Democedes, the pre-eminent physician of his time.

It is a revealing commentary to note that throughout the annals of history women have never outlived their vanity. Cosmetic considerations and false modesty have hindered the early diagnosis and timely treatment of breast cancer from the dawn of humanity until today. Since the breast has always been an aesthetic symbol of fertility and womanhood, amputation of the breast provoked mutilation of the mind as well as the body. Women have taken great pride in their breasts and formerly wore décolleté dresses with disarming propriety. Indeed it was was a customary and respectful form of salutation up until the seventeenth century to touch the breasts in a warm and friendly greeting. Thus, through the ages vanity has always been the deathtrap of reason in the diagnosis and treatment of breast cancer.

The Golden Era of Greek and Roman culture is associated with the Great Hippocrates who was born in the latter half of the fifth century B.C. on the Aegean island of Cos. Known as the ''Father of Medicine,'' Hippocrates (Fig. 3) represents all that is exemplary in the western tradition of medicine. Despite a prolific pen usually ascribed to Hippocrates and a vast collection of medical treatises which bear the name of Hippocrates, varying in content from the technical aspects of surgery to seven complete volumes of case histories, it is indeed curious that the treatment of cancer in general and breast cancer in particular received relatively little consideration.

It always comes as a startling revelation to find that many of our contemporary and cherished clinical observations have been so clearly described in ancient empirical works. For example, the ''Corpus Hippocraticum,'' referring to occult (nonulcerated or deep-seated) cancer makes this prophetic prognosis regarding the contraindications of surgery: ''It is better to omit treatment altogether; for, if treated, the patients soon die, whereas if let alone, they may last a long time.''

Among the aphorisms of Hippocrates (medical truths famous enough to have added a word to the English language) one finds: ''Those diseases that

medicines do not cure are cured by the knife. Those that the knife does not cure are cured by fire. Those that fire does not cure must be considered incurable." Referring specifically to cancer of the breast Hippocrates states: "A woman in Abdera had a carcinoma of the breast and bloody fluid ran from the nipple. When the discharge stopped she died." A second reference to breast cancer is found in the volume relating to "Diseases of Women":

> . . . and hard tumors appear in the breast, some large and some smaller, these do not suppurate, but continually grow harder and harder. From these grow hidden cancers. When cancers are about to come on, the mouth grows bitter, and everything they eat tastes bitter, and if you give them more to eat

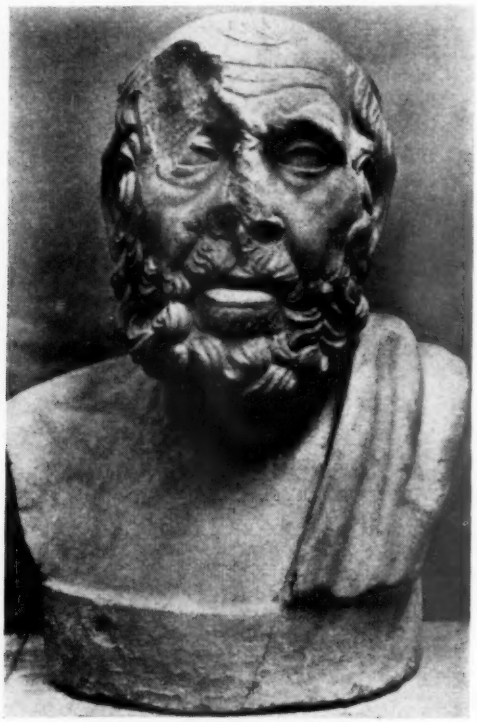


Fig. 3.—Hippocrates. From a head recently discovered near Rome and now in the Ostia Museum. (Courtesy of John Chadwick and W. N. Mann: Medical Works of Hippocrates, Springfield, Ill., 1951, Charles C Thomas, Publisher.)

> they refuse it, and shut their mouths. They become delirious, their eyes are hard and they do not see clearly, and pains dart from the breasts to the neck and beneath the shoulder blades, thirst seizes upon them, the nipples are dry, and the whole body becomes emaciated, the nostrils are dry and stopped up, and are not elevated with respiration. The breathing is superficial and they lose the sense of smell. Also they do not have pain in the ears, but sometimes convulsions. When they have gone as far as this, they do not recover, but die of this disease.

Aulus Cornelius Celsus, a Roman scholar of the early first century A.D., wrote an extensive encyclopedia on agriculture, medicine, military science, law, and philosophy of which there are only eight volumes on medicine still extant. Celsus knew a great deal more than his Hippocratic predecessors concerning the

natural history of cancer. He emphasized that irritation of cancer by the imprudent intervention of a physician could result in great danger to the patient. Yet despite his admonitions of caution there seems to be no doubt whatsoever that early Roman surgeons of this ancient time performed heroic surgery for cancer of the breast. In regard to amputation of the breast Celsus advised *against removal of the pectoral muscles* (an empiric procedure discarded during the Dark Ages only to be rediscovered and to find favor again almost 1,800 years later). He also warned against the use of both surgery and the cautery except in early cases where the progression from what the Greeks called a "cacoethes" to a carcinoma had not yet occurred.

> None of these can be removed but the cacoethes; the rest are irritated by every method of cure. The more violent the operations are, the more angry they grow. Some use caustics, some burning irons, others remove the growth with the scalpel. Nor was any person ever relieved by medicine; but burning exasperates and the growth spreads rapidly until it proves fatal; after excision, even though a cicatrix be formed it recurs, bringing with it the cause of death. Whereas, at the same time, most people, by using no violent methods to attempt the extirpation of the disease, but only applying mild medicines, to sooth it, protect their lives, notwithstanding the disorder, to an extreme old age. But no one can pretend to distinguish a "cacoethes" which is curable from a carcinoma, which is not, otherwise than by time and experiments.
>
> Therefore, as soon as this disease is perceived, caustic medicines ought to be applied; if the disorder is alleviated, and its symptoms grow milder, we may proceed both to incision and the actual cautery; if it is immediately irritated, we may conclude that it is already a carcinoma and everything acrid and severe is to be taken away.

Galen was a celebrated Greek physician who lived in the second century A.D. among the Romans and wrote with a remarkable prolixity. The vapors of Galen became the medical heritage of antiquity which clouded the path of progress for untold generations. The incredible authority of Galen and his sect created a dynasty of medical didactics during the Dark Ages which according to some medical historians may have been responsible for the refractoriness of medical progress until after the Renaissance. To question Galen was unorthodox heresy. In accord with his humoral theory of disease, Galen attributed cancer to an excess of black bile—melancholia. Cancer was therefore treated by a unique dietary regimen and purgation. However, if a breast tumor was readily removable, surgical excision was usually recommended.

> Cancerous tumors are found in all parts of the body, but particularly in the breasts of women, after the cessation of menstruation, which, so long as it is regular, preserves good health.

Galen's description of a breast tumor and the technique for its surgical removal was incredibly discerning:

> If you attempt to cure cancer by surgery, begin by cleaning out the melancholic tumor by cathartics. Make accurate incisions surrounding the whole tumor so as not to leave a single root. Let the blood flow and do not check it at once, but make pressure on the surrounding veins, so as to squeeze out the thick blood. Then treat as in other wounds.

We have often seen in the breast a tumor exactly resembling the animal called the crab. Just as the crab has legs on both sides of his body, so in this disease the veins extending out from the unnatural growth, take the shape of a crab's legs. We have often cured this disease in its early stages, but after it has reached a large size no one has cured it without operation. In all operations we attempt to excise a pathologic tumor in a circle, in the region where it borders on the healthy tissue. On account of the size of the vessels, especially when they happen to be arteries, there is immediate danger of hemorrhage, but if you use ligatures, extension of the disease to the surrounding parts takes place. If we elect to cauterize the roots of the tumor, there is also no small danger connected with this when the cauterization takes place close to important organs.

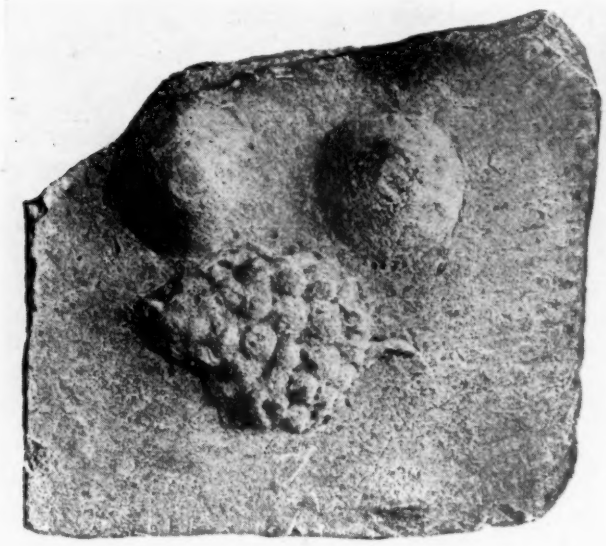


Fig. 4.—Limestone slab in the Cesnola Collection of the Metropolitan Museum of Art, New York. The stone relief was found in the temple at Golgoi, Cyprus, and dates from the Hellenistic period (third to second century B.C.). This votive offering seems to represent two breasts and a nodular tumor mass. It is perhaps one of the earliest representations of "cancer" in art.

According to the writings of Aetius, Leonides of the Alexandrian School was certainly a great physician, as well as an astute clinician and careful surgeon. Although his contemporaries were dominated by a nihilistic attitude toward cancer, Leonides performed courageous and skillful surgery in suitable cases. Careful not to operate in advanced cases, his original procedure for breast cancer is classic:

Placing the patient in the recumbent position, I make an incision into the sound part of the breast, above the cancer, and immediately apply the cautery until an eschar is produced to stop the bleeding. I then make another incision deep into the substance of the breast, and again apply the cautery, and so proceed—first cutting and then cauterizing alternately, in order to restrain the bleeding. So doing, there can be no danger of hemorrhage. When the amputation of the breast is completed again I sear the parts until they are quite dry. The first cauterizings are made for the purpose of arresting the hemorrhage, but the rest with the intention of eradicating the disease.

Leonides of Alexandria was also the first to describe nipple retraction as a most important clinical sign of breast cancer.

Aetius of Mesopotamia (Amida) also mentions ulcers of the breast and describes the difference between phagedenic ulcers and malignant ulcers. He notes that breast cancer may be ulcerated or not, but most often the breast tumor is hard and irregular, having extensive roots and accompanied by varicose veins. Pain may be generalized and penetrating. There is often sympathetic swelling and inflammation of the axillae, extending often to the collar bone and scapula. Poppyheads are recommended for the relief of pain.

The descriptions of many of these primitive and brutal operations are reminiscent of the martyrdom of Saint Agatha, the Patron Saint of Diseases of the Breast. Those who despair and doubt the progress of modern man may speculate regarding our present-day ingenuity. Has our genius outrun our character and compassion? Have we merely refined the art and by our cleverness improved the instruments of torture and weapons of brutality?

SAINT AGATHA, THE PATRON SAINT OF DISEASES OF THE BREAST

The legendary story of Saint Agatha starts in the third century A.D. on the island of Sicily. Born either in Palermo or Catania, she lived in the reign of the Roman Emperor Decius, during the seventh general persecution of the Christian Church. She came from a noble and illustrious family, and even early in life was considered destined to consecrate herself to God. From her earliest infancy Saint Agatha was preordained as a child of benediction.

However, her great beauty, charm, and social position soon captivated the heart of Quintianus, the Governor of Sicily. He deceitfully used the persecution of the Christians as a pretext for having her brought before his tribunal. His courtship spared no means to achieve its lustful designs. Yet Saint Agatha spurned his love and scorned the lover for his malice toward the Church. Failing thus to win her affection, Quintianus found her presumably guilty of Christian superstition and in reprisal ordered her into the house of Aphrodesia, a wicked woman of unsavory fame and questionable reputation. In this evil way he hoped to profane the Church and lead Saint Agatha from the path of Christian virtue and honor. However, during this period of imprisonment, Saint Agatha was resolute in her determination to maintain both her faith and her chastity.

After she had been kept captive for a month in this miserable brothel, Quintianus summoned Saint Agatha back to his court only to find that her faith in God was unshaken. Her life remained pure and undefiled and she continued to resist the amorous advances of Quintianus.

At this point in the martyrdom of Saint Agatha there exists a diversity of legendary lore, and several harrowing versions of Saint Agatha's torture are recorded. According to the most authentic of ancient traditions, Quintianus, in a backlash of anger, decreed that Saint Agatha "be bound to a pillar and her breasts be torn off with iron shears." She was then stripped of her garments and rolled naked upon potsherds, suffering the agony and anguish of cruel and prolonged torture. Finally she was cast into a dungeon to die, but the Lord

sent the Prince of his Apostles to heal her and restore her breasts. Quintianus, upon learning of the miracle of Saint Peter, was filled with rage and furiously directed that Saint Agatha be burned alive. But no sooner was she placed upon a blazing pyre than a violent earthquake shook the city of Catania. Believing that this scourge was inflicted upon their city because of the martyrdom of Saint Agatha, the people of Catania demanded that she be immediately released. Her torments at an end, she was placed in prison where she prayed to be allowed to die. The Lord then took her to Himself.

Fig. 5.—The martyrdom of Saint Agatha by Anthony Van Dyck. From the Bettmann Archive and Brit. J. Surg. 36: 116 (Oct.) 1948.

An equally colorful version of her exquisite sufferings places Saint Agatha upon a rack, with hot iron plates applied to her flesh and her breasts cruelly cut off. This brutal torment was accepted by the martyr with such equanimity and composure that Quintianus was infuriated. During that very night a venerable old man (Saint Peter) and a young child (Christ) visited Saint Agatha in her dungeon cell and, when they left, her wounds were healed and her breasts were restored.

Shortly thereafter the city of Catania was shaken by a violent earthquake, and two of the governor's most intimate friends were killed by falling masonry.

The people were in such a state of turmoil and excitement that Quintianus feared a general sedition unless Saint Agatha was liberated. However, she prayed to the Lord to receive her soul and on February 5 she died, and the Christians buried her with fitting benedictions and reverence.

One year after the death of Saint Agatha the city of Catania was threatened by a fulminating volcanic eruption from near-by Mount Etna. The devout and faithful Christians fled to Saint Agatha's tomb for refuge. There from among her sacred relics they took her veil, placed it on a lance and marched to meet the molten lava. The glowing mass was nearing the city when, suddenly confronted with the sacred relic, the lava swerved to one side and spared Catania. Skeptics, infidels, and heathens who witnessed this miracle promptly paid homage to the service of Saint Agatha and were baptized and converted to Christianity.

Fig. 6.—The martyrdom of Saint Agatha by Sebastiano del Piombo. (From the University Prints, Boston.)

Saint Agatha is regarded as one of the patronesses of the Western Church. She is both a saint and a martyr whose name is enshrined in the Litany of the Saints and in the Canon of the Mass. She appears in the old martyrology of Carthage and in all other martyrologies, both Greek and Latin. In the sixth century, Fortunatus mentions her in his poem on virginity as one of the celebrated Christian virgins and martyrs. In the Bible the Song of Solomon is said to foretell the brutal tortures of Saint Agatha. She is venerated as the patron saint of the Island of Malta and of the Sicilian cities of Catania and Messina. As the patron saint of the breast, wet nurses, and bellfounders, her aid is specially sought in all of the many diseases of the breast and in fire, colic, and dysentery, as well.

In art she is sometimes represented as bearing her breasts on a salver. These have been mistaken for loaves of bread and thus arose the custom of blessing bread on Saint Agatha's Day. In Scandinavian countries it is believed that

Quintianus had Saint Agatha brushed to death. Therefore, on February 5, Saint Agatha's Day, it is traditional for girls to abstain from brushing their hair.

In regard to the medical treatment of breast cancer, the ancients appeared to have tried many medicines—mineral, vegetable, and animal—as well as innumerable psychic and physical agents, all of these, of course, without success. Caustics were skillfully used by the Egyptians, Greeks, and Romans, and this art was especially well developed by the Arabian School of Medicine. Since religious taboos prohibited Islamic physicians from engaging in dissection and most likely surgery, the use of caustics was frequently employed with considerable zeal. "In the presence of a disease which constantly terminates in death the physician's duty consists in boldly trying everything."

DARK AGES

In the Dark Ages the medical writers were primarily concerned with the didactic dogmas and theories of treatment of their ancient predecessors. These rudimentary concepts of medicine were frequently analyzed, discussed, and compared so as to dispose of any apparent contradictions. So firm was their faith in Galen that when Vesalius during the Renaissance clearly proved that Galen's concept of the hip bones was wrong, it was contended by the sixteenth century physicians that man had since changed his shape as the result of wearing tight trousers. Thus, the prospect of progress in the knowledge of medicine was hardly more than a languishing ray of hope. Typical of these ancient times was the statement that Apollo discovered medicine, Aesculapius extended the knowledge of medicine, and that Hippocrates perfected it. The precepts of Hippocrates and the gospel of Galen were emulated by the empiricists and the evolution of medical science remained in abeyance.

Albucasis, Cordova's celebrated Spanish-Arabian surgeon, born A.D. 1013, had his doubts about the value of surgical treatment for cancer. If the cancer lies in a locality where it can be grasped in toto like the mammary gland, and especially if not fully developed, operation may be attempted. Though he says, "As for me I have never been able to cure a case nor have I known of one who has."

Lanfrank (A.D. 1296), the father of French surgery, was still using the method of Leonides in the treatment of breast cancer despite a lapse of more than one thousand years. Henri de Mondeville (A.D. 1320) favored deep incision, extirpation, and cauterization in small cancers, whereas arsenic and zinc chloride caustic pastes were the treatment of choice in large cancers. A unique method of treatment was employed by the Spanish surgeon, Francisco Arces (1493), who divided the cancerous breast lengthwise and dissolved the tumor by means of a ligature. Leonard Fuchs (1501), a German physician and surgeon, compressed cancers of the breast by means of a lead plate. The merit of Guy de Chauliac (1300 to 1367) in the treatment of cancer rests upon his authoritative surgical text, *Chirurgia Magna.* Conservative treatment including purgation and a dietary regimen were recommended. If a tumor seemed operable, a wide excision was performed including the removal of all the "rests."

The great army surgeon, Ambroise Paré (1510 to 1590), was a Galenist and conservative in the treatment of cancer. If the cancer was small, nonulcerated, and situated in a region where it could easily be removed, he excised the tumor, taking care to go well beyond its boundaries. Large and ulcerated lesions were treated with sweet milk, vinegar, and ointments. Paré, however, recognized a relationship between breast cancer and axillary extension of the disease. Andreas Vesalius (1514 to 1564), a renowned Belgian anatomist in the early Renaissance period, lectured in Padua, Basel, Pisa, and Bologna and spent the later years of his life as savant and body physician to the Imperial Court of Spain. He was one of the first to oppose Galen's doctrines vigorously and to discard the old anatomy. The publication of the *De Humani Corporis Fabrica* in 1543 marks the beginning of modern anatomy and represents an exquisite piece of creative art. Vesalius treated cancer by wide surgical excision and controlled bleeding by means of ligatures.

Fabricius ab Aquapendente (1537 to 1619) was an Italian surgeon and anatomist, famed as a professor at Padua and teacher of William Harvey. He performed radical surgery for cancer only at the patient's request, and decried partial excisions as worthless.

An early contributor to the differential diagnosis of benign and malignant breast tumors was Marcus Aurelius Severinus (1580 to 1656) of the School of Salerno. He favored removing benign breast tumors because of the possibility of their becoming malignant. He was one of the first surgeons to remove enlarged axillary nodes at the same time he radically excised breast cancer.

Nicolaes Tulp (1628 to 1653) was a Dutch anatomist and surgeon, professor of the Surgeons' Guild in Amsterdam. He commissioned Rembrandt to paint the now famous "Anatomy Lesson" showing Dr. Tulp during an anatomy demonstration. He believed that breast cancer was contagious and described a case in which the disease was passed presumably from mistress to her servant girl.

William Clowes (1560 to 1634), physician to Queen Elizabeth, resorted to exorcism in the cure of breast cancer. The simple ritual of laying on the royal hands was the queen's counterpart of curing the king's evil. The "royal touch" was said to have originated with Edward the Confessor, but several of his successors were somewhat skeptical of their own divine power of faith healing. William III possessed no self-delusion when he told his ailing subjects, "May God give you better health and better sense." Finally he refused to continue the practice and was consequently accused of cruelty. Queen Elizabeth had a blessed ring which she wore suspended between her breasts. This ring had "the virtue of expelling infected air" and preventing disease. Similar amulets of asafetida were worn until recent times.

Although the first accurate appreciation of the nature of cancer and its differentiation from other conditions had to await the development of the microscope, yet the early methods of mastectomy though barbarous and crude were surprisingly efficient and probably the result of expediency at a time when speed was of the essence. Scultetus (1595 to 1645), a famous illustrator of surgery and surgical instruments, gave a very vivid portrayal of the operative procedure for cancer of the breast (Fig. 7). Heavy ligatures were passed

through the base of the breast, traction was then applied as the breast was swiftly amputated, and bleeding from the operative area was quickly seared with a hot iron.

Gerard Tabor invented an instrument to expedite and simplify the rapidity of mastectomy. This instrument was used in amputation of the breast for cancer.

The Reverend John Ward, who was Vicar of Stratford-on-Avon from 1662 to 1682 and was at heart a surgeon and pathologist, was quoted by Sir D'Arcy Power:

> A cancer in Mistress Townsend's breast of Alveston, taken off by two surgeons, the one's name was Clerk of Bridgnorth, the other's was Leach of Stourbridge. First, they cut the skin across and laid it back; then they worked their hands in it, one above, the other below, until their hands met and so brought it out. They had their needles and waxed threads ready but never used them, and also their cauterising irons, but they used them not. She lost not above six ounces of blood in all.

MODERN MEDICINE

One of the most enlightened surgeons of the eighteenth century was Henri Francois le Dran (1685 to 1770). His concept of cancer was of great importance because he completely repudiated Galen's humoral theory of the disease in favor of the idea that cancer was a local lesion in its earliest stage. Le Dran believed cancer spread by way of the lymphatics to the regional nodes and he clearly described the path of metastases from breast cancer. He recognized the need for early operation. He dissected out enlarged axillary nodes in breast cancer, and was aware of the fact that the hope of cure was decidedly less when the axillary nodes were involved.

Jean Louis Petit (1674 to 1750), a famous French surgeon and the first Director of the French Surgical Academy, set the precedent for modern mastectomy. He believed that the roots of a cancer were the enlarged lymphatic glands, that the glands should be looked for and removed, and that the pectoral fascia and even some of the fibers of the muscle itself should be dissected away rather than leave any doubtful tissue. Petit's "Traite des Operations" was not published until twenty-four years after his death; however, his teachings were widely disseminated by his students and contemporaries. Although the breast tumor itself was carefully avoided during the operation, as little skin as possible was removed with preservation of the nipple. When breast cancer was sufficiently extensive to involve the overlying skin he recognized the need for block dissection: "Where the integuments are also affected and strictly joined to the cancer there is little hope to expect a perfect cure if they are not both cleanly extirpated together." When the cervical or supraclavicular nodes were involved Petit considered the prognosis poor indeed. The surgical skill and anatomic knowledge of Petit place him in a position of pre-eminence as an early eighteenth century master surgeon. His careful removal of the axillary nodes, his wide surgical excision of the primary tumor, and his appreciation of dissection in continuity at a time when major surgical procedures so often resulted in

widespread infection and death, indicated a vision far ahead of his time and a valor for timely and thoughtful treatment.

The pessimism of the period, however, is expressed by Alexander Monro, who laments that of sixty cases of breast cancer treated surgically only four were free of the disease at the end of two years. In reviewing the literature Velpeau (1856) notes that, "To destroy a cancerous tumor by surgical means is

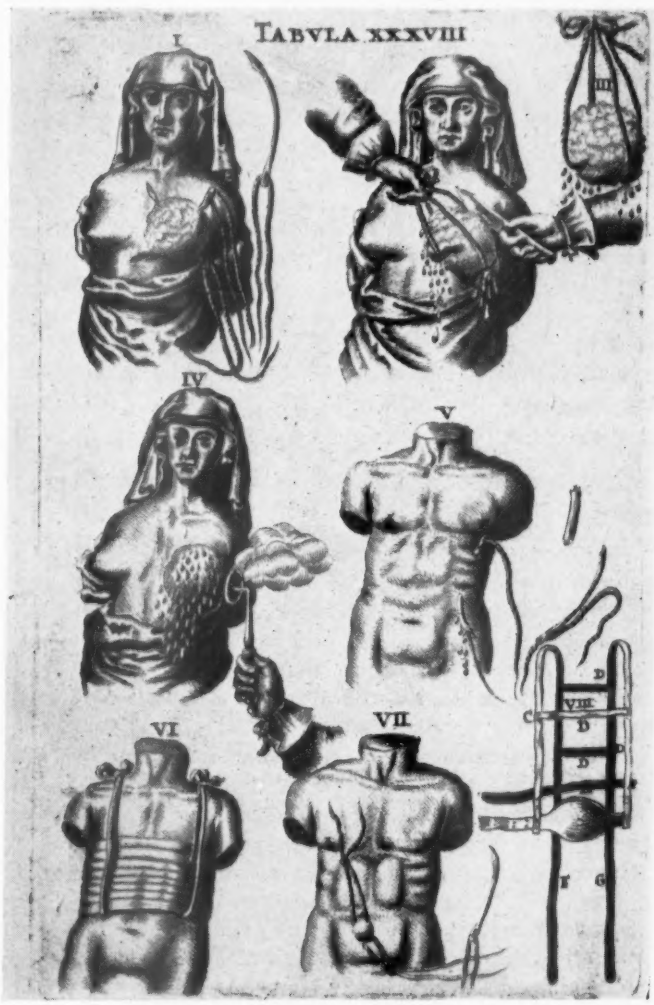


Fig. 7.—The operative procedure for cancer of the breast as vividly illustrated by Scultetus (1595 to 1645). The Scultetus binder—an eponymic and effective abdominal support still in surgical use—is shown in the lower left-hand corner. (From Scultetus, Johannes: Armamentarium Chirirgicum, A. Vlacq., 1655.)

usually an easy matter, and but little dangerous in itself; but the question arises, whether such a proceeding affords a chance of radically curing the patient. This proposition is still undecided, although it has been discussed since the time of Hippocrates." According to some observers, Velpeau continues, "the disease always returns after removal, and operation only accelerates its progress and fatal termination. This also was about the opinion of Boyer, who, out of 100

operations, could enumerate but four in which there was a permanent cure. Scarpa, who met with but three cases of complete success; Mayo, who speaks of ninety-five cases of return in 100 operations; and MacFarlane, who, out of 118 operations, knew not of a single positive cure. . . ." However, Velpeau contends that these pessimistic views cannot be the result of rigorous observation. The backward state of science at the time "prevents our attaching great importance to their views."

Benjamin Bell, surgeon to the Edinburgh Royal Infirmary, elaborated upon the views of his predecessors in his surgical system published in 1784. In considering amputation of the breast for cancer, he taught that

> . . . when practitioners have an opportunity of removing a cancerous breast early they should always embrace it; that as little skin as possible should be removed, and that the breast should be dissected off the pectoral muscle, which ought to be preserved. If any indurated glands be observed they should be removed and particular care should be given to this part of the operation, for, unless all the diseased glands be taken away no advantage whatever will be derived from it. Even when only a small portion of the breast is diseased the whole mamma should be removed. The axillary glands should be dissected out by opening up the armpit, but as much skin as possible should be preserved. I have done this since 1772. The older surgeons took away the skin and left the glands.

James Syme (1799 to 1870), a Scottish surgeon, writing in his "Principles of Surgery" in 1842 condemned the practice of palliative procedures in the treatment of cancer.

> The only proceeding that deserves at all to be considered a remedy for cancer is removal of the morbid structure. This may be done sometimes by the actual or potential cautery, but these means are very apt to destroy the disease only partially and consequently do no good, but on the contrary harm, by exciting greater activity in the portion that remains.
>
> The knife or scissors effect the extirpation most easily and securely. It would be subjecting the patient to useless pain and would bring surgery into discredit to attempt extirpation in cases where the extent or connection of the disease prevented its complete removal. It is also incumbent upon the surgeon to search very carefully for glands in the course of the absorbents that may become affected since it appears that the result of operations for carcinoma when the glands are affected is almost always unsatisfactory however perfectly they may seem to have been taken away. The reason of this probably is that the glands do not participate in the disease unless the system is strongly disposed to it and consequently their removal, however freely and effectually executed, cannot prevent the patient's relapse.

Syme then recommends wide excision and complete resection wherever possible, "the whole of it ought always to be removed however small the part of it which is externally affected may be and when the tissue concerned is not in this way circumscribed, the knife should be carried as wide as possible from the tumor."

At a time when extensive surgery was frequently followed by fulminating infection, when anesthesia was yet in its infancy, and when long-term cancer survivals following operation were a clinical curiosity, it is indeed no wonder that amputation or mastectomy was advocated only by those with a stout heart

and unquenchable optimism. The first true appreciation of the basic nature of cancer and its differentiation from other conditions had to await the development of the microscope. Schleiden, in 1838, was among the first to appreciate the significance of the cell as a unit in plant structure, and Schwann in the following year recognized similar units in animal tissue. Müller noted the cellular structure of neoplasms. Although some believed that cells could be created from formless intercellular substances, Remak (1852) discovered cell division and Virchow and Leydig epitomized the matter by saying, "omnis cellula e cellula." The great pathologist Virchow advanced the concept that any normal cell could become a cancer cell as the result of irritation. Müller taught the fatalistic view that cancer originated in cells which were abnormal at birth. In an atmosphere of uncertainty and conflict regarding the origin and treatment of cancer it was inevitable that this vacillation should be reflected in the conservative versus radical operative attack on breast cancer. Prevailing pessimism indicated that the most one could ever expect from an operation for breast cancer was that the patient might die a little less miserably.

Sir James Paget (1814 to 1899), writing in 1853 at the dawn of surgical pathology and prior to the widespread scientific blessings of anesthesia and asepsis at a later date, suggested that, "we have to ask ourselves whether it is probable that the operation will add to the length or comfort of life, enough to justify incurring the risk for its own consequences." In 235 cases of breast cancer there was an operative mortality of 10 per cent. There follows an eloquent dissertation on the indications and contraindications for mastectomy in a disease which seemed to him to be hopeless. Speaking of seventy-four cases collected by himself and M. Lebert he notes that:

> Neither of us has yet seen a case where recurrence was delayed beyond eight years.
>
> In deciding for or against the removal of a cancerous breast, in any single case, we may, I think, dismiss all hope that the operation will be a final remedy for the disease. I will not say that such a thing is impossible; but it is so highly improbable, that a hope of its occurring in any single case cannot be reasonably entertained.

Robert Liston (1794 to 1847), writing at about the same period, was equally disconsolate about the advantages of mastectomy:

> Recourse may be had to the knife in some cases but the circumstances must be very favourable indeed to induce a surgeon to recommend or warrant him in undertaking any operation for the removal of malignant disease of the breast. When the disease has been of some standing there is a considerable risk of the axillary glands having become contaminated. No one could now be found so rash or so cruel as to attempt the removal of glands thus affected whether primarily or secondarily.

A. Velpeau, a famous French surgeon with the opportunities for observation of a tremendous clinical practice, wrote an excellent *Treatise on the Diseases of the Breast* in 1856. The chief value of the book lies in its practical character. Written at a time when the inauguration of microscopic pathology was setting the profession astir, it represents the views of the "old guard" who

hesitated to accord complete faith to the new cell doctrines. Regarding the operative treatment of breast cancer Velpeau favored thorough excision in preference to complete amputation:

> If the disease require it, the pectoralis major muscle should not arrest us. The smallest shade of the disease must be taken away, if we are determined not to lose any chance of success. However, should there appear to be the necessity of interfering with the bones, or resecting the ribs, we must not deceive ourselves. The return of the disease is then inevitable, and it would have been better not to have undertaken the operation at all.

The operative procedure of Velpeau consisted in complete excision of the tumor with its overlying skin (with preservation of the nipple when possible) and only in certain cases amputation of the breast.

> If a considerable portion of the mamma is affected, it is better to remove the whole gland than to preserve a few of its lobes. Some surgeons have stated that, as a general rule, the whole mamma should be sacrificed in a case of cancer. No matter how small the tumour may be, I have often heard M. Roux say that the return of the disease is almost certain, if we remove merely a portion of the parenchymatous organ in which a cancer happens to be situated, in place of amputating the whole. However, notwithstanding my respect for M. Roux, I cannot coincide in his opinion on this subject.

The general or local nature of cancer excited considerable interest as well as the relationship and differentiation between benign and malignant breast tumors.

New ideas which are the seeds of medical progress are said to be acquired privately, but they must be cultivated publicly. Thus, Charles H. Moore, a keen clinician and surgeon to the cancer wards of the Middlesex Hospital, presented to the professional public a most important and timely paper at a meeting of the Royal Medical and Chirurgical Society in London in 1867. Following a careful clinical investigation of the reasons for failure and recurrence following operations for breast cancer Moore planted his seeds of learning among a fertile and enlightened audience in a paper entitled, "On the Influence of Inadequate Operations on the Theory of Cancer." Moore concluded that:

> Local recurrence of cancer is due to the continuous growth of fragments of the principal tumour. Such recurrence may take place also in a residual part of the organ, respecting which it cannot be asserted that it was cancerous at the time of the operation. Such recurrence may further happen in a structure adjoining a completely extirpated breast, and on a comparison of cases may be held to be produced by disseminated fragments of the original tumour.

After a discussion of extension of the disease to the axilla Moore continued:

> It is not sufficient to remove the tumour, or any portion only of the breast in which it is situated; mammary cancer requires the careful extirpation of the entire organ. The situation in which the operation is most likely to be incomplete is at the edge of the mamma next to the sternum. When any texture adjoining the breast is involved in or even approached by the disease, that texture should be removed with the breast. This observation relates especially

to skin, to lymphatics, to much fat, and to pectoral muscle. The attempt to save skin which is any degree unsound is of all errors perhaps the most pernicious, and whenever its condition is doubtful, that texture should be freely removed.

In the performance of the operation it is desirable to avoid, not only cutting into the tumour, but also seeing it. No actually morbid structure should be exposed lest the active microscopic elements in it should be set free and lodge in the wound. Diseased axillary glands should be taken away by the same dissection as the breast itself, without dividing the intervening lymphatics; and the practice of first roughly excising the central mass of the breast, and afterwards removing successive portions which may be of doubtful soundness, should be abandoned. Only by deliberately reflecting the flaps from the whole mamma, and detaching it first at its edge, can the various undetected prolongations of the tumour and outlying nodules be included in the operation.

Thus, Moore in 1867 had postulated the cardinal principles of radical mastectomy except for the essential excision of the pectoral muscles.

In commenting upon the past performance of inadequate mastectomy Moore stated:

Taught without doubt by foregoing failure our surgical ancestors adopted a method that might well have been expected to prove effectual against a local recurrence of the disease. They transfixed the base of the mamma and raising it with ligatures swept off the whole organ together with the skin that covered it. The proceeding had a barbarous appearance enough, but it was promising and if their knowledge of the disease had led the surgeons of the time to adopt it before the skin was hopelessly infiltrated they must have met with more success than they appear to have done.

It was mistaken kindness which led to a change of this mode of operating. Under the influence of a clergyman who expressed what must have been the prevailing horror at such Amazonian surgery, the practice was changed to an incision in the integument which was reflected in flaps and brought together again after removal of the cancerous tumour. There could have been no decrease in suffering by the prolongation of the operation and what was gained by it in neatness was lost in life.

In setting forth this epoch-making treatise Moore received a somewhat less than triumphant acclaim from his professional colleagues. For a "man gazing on the stars is proverbially at the mercy of the puddles on the road."

Three years later, however, Joseph Lister (1827 to 1912) fostered the observations of Moore and enhanced the operation by refining the technique of axillary exposure. Lister divided but did not remove the pectoral muscles:

Thus I have at present a patient about to leave the infirmary three weeks after the removal of the entire mamma for scirrhus, all the axillary glands having been at the same time cleared out after division of both the pectoral muscles, so as to permit the shoulder to be thrown back and the axilla freely exposed, as is done in the dissecting room—a practice which I have for some years adopted where the lymphatic glands are affected in that disease. In this case a great deal of care was certainly required for the first few days; but after a week the dressings were only changed once in three days, and when a fortnight had elapsed, cicatrization being almost perfect, a week was allowed to pass without any interference. Hence, on the whole, the labour was considerably less than with ordinary treatment, and a very much greater amount of pain

would have been amply repaid by the beautiful linear cicatrix, formed without the occurrence of one drop of pus, and without any serious constitutional disturbance.

In 1877 Mitchell Banks read a paper before the Lancashire and Cheshire Branch of the British Medical Association entitled, "A Plea for More Free Removal of Cancerous Growths" in which he attacked the problem that too few surgeons were practicing "extensive and sweeping removal" of breast cancer. Continuing his interest in this "hobby" of breast surgery, Banks reported the results of his operative treatment in 1882:

> Surgeons, as a rule, do not remove cancers of the breast. They persuade their patients that they do, and they almost persuade themselves. But there is always that little bit which they leave behind, and which they fondly hope will not grow, because it is such a little bit. Alas! that so little leaven should leaven the whole lump!

Later in the same presentation he continued:

> In the present paper a principal object is to advocate the removal of the axillary glands, as well as the breast, in all cases, whether we can feel them enlarged or not—in fact, to make a clearing out of the axilla a necessary part of the operation for removal of the breast. I have been quietly practising this for three or four years, having been driven to the conclusion that it was the right thing to do, by discovering that, even in those cases where certain glands could distinctly be felt enlarged, when the axilla was opened, small ones were quite incapable of being felt from the outside. . . . I beg leave, therefore, gentlemen, most strongly to urge the invariable clearing out of the axillary glands along with the removal of the breast, the one operation being useless without the other. As you cannot tell whether the glands are affected or not till you see them in your hand, let them be always removed, and so increase the patient's chances of future immunity.

Concerning the use of Listerian antiseptics, Banks had this to say:

> As a rule, I employ them; in hospital always. But in the operation under consideration, they have this one great disadvantage, that the spray seriously cools down the patient, and thus lowers her vitality. If the operation is performed in the old-fashioned and thorough and sweeping way I am now advocating, there is a serious shock, seeing that from thirty to forty minutes is the very shortest time in which it can be satisfactorily done. Now, let any healthy woman get out of a warm bed, strip herself naked to the waist, and then go and lie down on her kitchen table for forty minutes, and I shall be very much surprised if she has not a cold next day. But in addition to this let a cold spray play upon her, and furthermore let a great mass of heat-conserving skin and fat be carried away from the chest, so that nothing but ribs and muscles intervene between the lung and the air; and still let the cool spray play upon her. Is not this likely to be very depressing? I am convinced that it is so; and if the operator, in place of doing his work rapidly, niggles and fiddles about it, so that the patient is kept for a long time under the combined lowering influences of cold spray, anaesthetic, and loss of blood, then the result is that a distinct catarrhal pneumonia very speedily appears. And this I have seen put the patient's life in imminent jeopardy on several occasions. For this reason, in private, where there is but little fear of septic influences, if the patient be weakly I content myself with simply washing out the wound well with carbolic solution and maintaining a modified antiseptic dressing. In

> hospital I do not use the spray till the operation is pretty well completed, when I turn it on for a minute or so, and drench all the parts well before the final stitching up is done.

Dr. Joseph Pancoast (1805 to 1882), Professor of General Descriptive and Surgical Anatomy at Jefferson Medical College in Philadelphia, was one of the earliest American surgeons to emphasize the importance of excising the breast and glands in one piece, but he made no mention of dividing the pectoral muscles to gain better access to the contents of the axilla. Pancoast's successor at Jefferson Medical College was Samuel D. Gross, Professor of Surgery, who advocated amputation of the breast but sacrificed thoroughness for conservation of skin and preservation of the axilla. Samuel W. Gross, his distinguished son, subsequently amended the surgical omissions of his father by publishing, in 1880, an excellent book entitled *Tumors of the Mammary Gland*. He sponsored the radical operation of Mr. C. H. Moore in the United States and extended it to include excision of the pectoral fascia.

> In a remarkable paper . . . Mr. Moore, of London, in 1867, enunciated certain doctrines which, had they been widely circulated and appreciated at their full value, would possibly ere this have demolished the antiquated and utterly false teachings as to the incurability of carcinoma.

Samuel W. Gross was convinced that breast cancer could be cured by thorough operations performed "before it has disseminated itself extensively locally or has tainted the general system." He believed that "the proper procedure is to remove the entire breast and its coverings by a circular incision, search for any outlying lobules that may be disseminated throughout the mammary region, dissect off the fascia of the pectoral muscle, and prolong the outer portion of the incision into the axilla with a view to its thorough exploration." The wisdom of this modern doctrine was amply confirmed by careful histologic study.

Although the skills of manual dexterity and surgical courage have been the attributes of surgeons for many, many generations, modern progress in surgery in general and cancer surgery in particular awaited the development of (1) a knowledge of anatomy and microscopic anatomy, (2) a satisfactory method of hemostasis, (3) anesthetics for the relief of pain, and (4) the development of antiseptic and later aseptic surgical techniques for the control of infection. Prior to this period the results of the surgical treatment of breast cancer could hardly be called gratifying. D. Hayes Agnew (1818 to 1892) resorted to surgery solely for its morale effect. He believed that operation actually shortened rather than prolonged the survival time.

The triumph of hope over case histories—of the scientific spirit over the Dark Ages—was sufficient to stir the souls of a group of German surgeons who devoted a great deal of zeal and study to the development of an improved operation for the treatment of breast cancer. Volkmann writing in 1875 said, "I make it a rule never to do a partial amputation for cancer of the breast, but remove the entire breast, even for the smallest tumors, and at the same time I take away a liberal piece of skin." This leading surgeon of the German School carried his incision down to the pectoral muscle and dissected the fibers cleanly,

"carrying the knife parallel with the fibers of the muscle and penetrating into their interstices. The pectoralis fascia is thus entirely removed. I was led to adopt this procedure because, on microscopic examination, I repeatedly found when I had not expected it that the fascia was already carcinomatous, whereas the muscle was certainly not involved."

The pectoralis major and at times the pectoralis minor muscles were excised by Volkmann in thirty-eight patients all of whom had far advanced cases of breast cancer. In 14 per cent of these patients he noted a three-year survival without evidence of recurrence. Judging from the rather meager accounts of operative breast surgery as practiced at the time of Volkmann, Billroth and Heidenhain were perhaps the only other prominent German surgeons who had the courage and conv[illegible]n to remove the pectoral muscles for breast cancer.

Heidenhain supported the work of Volkmann when he wrote (1889):

> I am firmly convinced from what I have seen that carcinomata when they have actually made their way into the lymphatic channels, which is usually the case, have always sent their advance guards to the surface of the muscle, no matter what thickness of fat lies between the breast and the muscle; in other words, that a tumor, however freely movable on the underlying parts, has almost certainly advanced as far as the surface of the muscle.

Heidenhain believed that cancer cells were frequently propagated through the lymphatics by muscular action. Where breast cancer had become adherent to the pectoral muscles he advocated excision of the involved muscles. In a careful microscopic study of eighteen cases of breast cancer he found it impossible to eradicate the disease without excision of the superficial layer of the pectoralis major.

Thus, although the seeds for the complete radical operation for breast cancer were already planted in the minds of many men, it remained for Dr. William Stewart Halsted to culminate the operation and germinate the present modern method. The fertile mind of Halsted was, so to speak, made up of all the minds of the preceding ages.

Concealed within the text of an article on wound healing, Halsted first published in 1890-1891 a summary of thirteen cases of breast cancer with a description of his surgical technique. In commenting upon the operation which now bears his name Halsted said:

> About eight years ago (1882) I began not only to typically clean out the axilla in all cases of cancer of the breast but also to excise in almost every case the pectoralis major muscle, or at least a generous piece of it, and to give the tumor on all sides an exceedingly wide berth.

Halsted then points out the difficulty in determining by gross examination alone whether or not cancer has invaded the pectoral muscle.

> From the careful microscopical examination of many very small cancers of the breast I am convinced that the pectoralis major muscle is usually at the time of the operation involved in the new growth. Strange to say, no authority so far as I know suggests the advisability of always removing the pectoralis muscle or a portion of it in operations for the cure of cancer of the breast; and still stranger there are many surgeons of the first rank—surgeons in favor of

> methodically cleaning out the axilla—who instead of recommending the excision of the muscle advise the removal of the fascia only from the pectoral muscle. . . . Surely it is absurd not to remove the muscle when its fascia is, even to the naked eye, diseased.

In 1894 Halsted presented before the Clinical Society of Maryland the results of the complete operation for the cure of cancer of the breast performed at the Johns Hopkins Hospital. The basic principles of this operation "which has been attended with such surprisingly good results in our hands" were logically conceived and featured two principal premises:

> The pectoralis major muscle, entire or all except its clavicular portion, should be excised in every case of cancer of the breast, because the operator is enabled thereby to remove in one piece all of the suspected tissues.
>
> The suspected tissues should be removed in one piece (1) lest the wound become infected by the division of tissues invaded by the disease, or of lymphatic vessels containing cancer cells, and (2) because shreds or pieces of cancerous tissue might readily be overlooked in a piecemeal extirpation.

In establishing so sound a reason for removing the pectoralis major muscle it is strange indeed that Halsted neglected the underlying pectoralis minor muscle and considered it worthy of salvage. Yet in 1894 Halsted's recommended operative procedure merely divided the minor muscle at right angles to its fibers and meticulously cleaned away the "loose connective tissue which seems to be rich in lymphatics and contains more or less fat. This fat is often infiltrated with cancer."

Four years later (1898) Halsted reported "A Clinical and Histological Study of Certain Adenocarcinomata of the Breast" and noted:

> Our present method of operating for the cure of breast cancer is even more radical than it was at the time of the writer's first publication on this subject. The supraclavicular region is almost invariably cleaned out. To do this we no longer divide the clavicle as we did five or six years ago.

Other changes of importance at that time included the excision of both pectoral muscles and the immediate grafting of all operative wounds.

The proponents of the present trend toward ultraradical breast surgery might very well trace the origin of these operations to the early disciples of Halsted.

> Dr. Bloodgood, Instructor in Surgery, has, on the necks of two patients, done as many as three operations each for glandular involvement, and apparently saved his patients. The additional operations were for glands above and below the region of the neck first attacked. In one of these cases he entered the mediastinum from above to remove a cancerous gland, and had to excise a piece of the innominate vein. Dr. H. W. Cushing, my house-surgeon, has in three instances cleaned out the anterior mediastinum on one side for recurrent cancer. It is likely, I think, that we shall in the near future remove the mediastinal contents at some of our primary operations.

For extensive disease Halsted favored stripping the sheaths of the rectus, serratus anterior, subscapularis, as well as the latissimus dorsi and teres major "A part of the chest wall should, I believe, be excised in certain cases. . . ."

Then as now the dangers of delayed diagnosis were well recognized by Halsted:

> I wish it were possible to enlighten the people, as well as the physicians in all parts of this country, on the subject of breast cancer, and make them realize how important it is that the operation should be done as soon as the tumor is discoverable.

In 1907 Halsted presented "The Results of Radical Operations for the Cure of Cancer of the Breast" in which his initial enthusiasm for supraclavicular dissection seemed tempered by experience. The supraclavicular operation was omitted in 113 of 232 later cases. "Before accepting the statement of any-

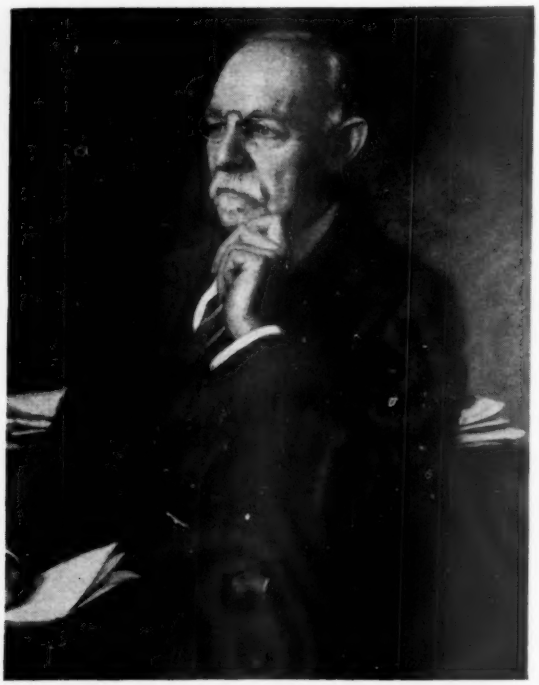


Fig. 8.—Portrait of Dr. William Stewart Halsted by Mr. Thomas Corner. This picture is in the lobby of the Halsted Surgical Building of the Johns Hopkins Hospital, Baltimore, Md.

one that he has cured a case of breast cancer with neck involvement, incontrovertible proof should be demanded." Although Halsted still believed that it was "incumbent upon the surgeon to perform in many cases the supraclavicular operations," yet he remained skeptical as to the cure.

In a letter to Dr. William H. Welch dated Aug. 26, 1922, Halsted appraised with characteristic modesty his own contribution to the original conception of radical mastectomy:

> I advised and practised the removal of the entire muscle, leaving in most instances the upper or subclavicular bundles (those above the cephalic vein); I divided the pectoralis minor to further facilitate the cleaning of the axilla. A year or two later Willy Meyer advised removing the minor muscle as well as the major, and I, too, came independently to the conclusion that this might better be done. I insisted that all the tissues should be removed in one piece

and upon the meticulous cleaning of the axilla and its aestuaries (subclavicular and supraclavicular fossae). I warned of the danger of excising pieces of malignant tumors for microscopic examination unless the operation followed immediately, and was, I think, one of the first surgeons in this country able macroscopically to make the diagnosis of the common tumors.

Contemporaneous with the publication of Halsted's second paper describing in detail his method of mastectomy in November, 1894, Willy Meyer presented his improved operation for breast cancer before the New York Academy of Medicine. Both surgical techniques were independently conceived but were essentially similar. There was no mutual indebtedness. Willy Meyer advocated the routine removal of the pectoralis minor muscle, an amendment acknowledged by Halsted and readily accepted in his subsequent surgical technique. The two operations were almost identical except for the skin incision, removal of the pectoralis minor muscle, and the direction of the dissection. The essence of Willy Meyer's radical operation endeavored "to extirpate the breast, the contents of the axillary and of the sub- and infra-clavicular region, and the pectoral muscles, in one mass."

Whereas Willy Meyer had operated on only six patients within the three years preceding his report, Halsted had had the opportunity of operating on more than fifty patients and had apparently started his studies some twelve years prior to his 1894 report of end results. Thus, although precedence for the radical mastectomy clearly belongs to Halsted, the originality of both of these master surgeons served to focus the attention of the profession upon the basic principles of the modern radical mastectomy.

Certainly one of the most fascinating features of the legend and romance of medical history is the way in which new ideas often arise simultaneously in the minds of many men. Although the progress of medicine may be zigzag it is never random. Whyte has recently called attention to the inexorable order that prevails in the world of science and culture and has briefly listed the best known examples of contemporaneous discovery. "The telescope was claimed by nine inventors, the thermometer by five, and nearly every major electrical invention up to the present day has involved a race for priority." In the field of medicine alone, Stern has noted some two hundred examples of simultaneous discovery. Vaccination was not a distinctive innovation of Jenner. The immunity to smallpox which cowpox afforded was widely known at the time both in England and on the Continent. Vaccination had been performed by Jesty in 1774, Jenson and Plett in 1791, and finally by Jenner in 1796. "Curling's ulcer" was actually described by Dupuytren in 1832 some ten years before Thomas Curling's report appeared. Wells (1811) and Blackall (1813) had established the correlation between dropsy and albuminous urine long before Richard Bright—one of the "great men of Guys"—gave his celebrated account of nephritis. Childbed fever was independently considered a contagious or infectious disease by Oliver Wendell Holmes in the United States, Semmelweiss in Vienna, Tarnier in Paris, and Lister in London within a relatively short time of one another.

Goethe, as early as 1793, said that "the most beautiful discoveries are made not so much by men as by the period. . . . They mature in the course of time just as fruits fall from the tree at the same time in different gardens." Thus, many innovations seem destined to be by virtue of both a man and a moment. Emerson's essay on Fate reminds us that, " 'Tis frivolous to fix pedantically the date of particular inventions. They have all been invented over and over fifty times. . . . Man is the arch machine of which all these shifts drawn from himself are toy models. 'Tis hard to find the right Homer, Zoroaster or Menu; harder still to find the Tubol Cain, or Vulcan or Cadmus or Copernicus, or

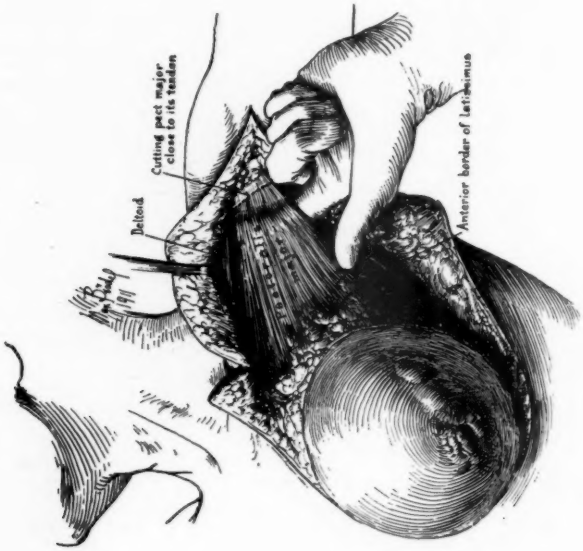


Fig. 10.

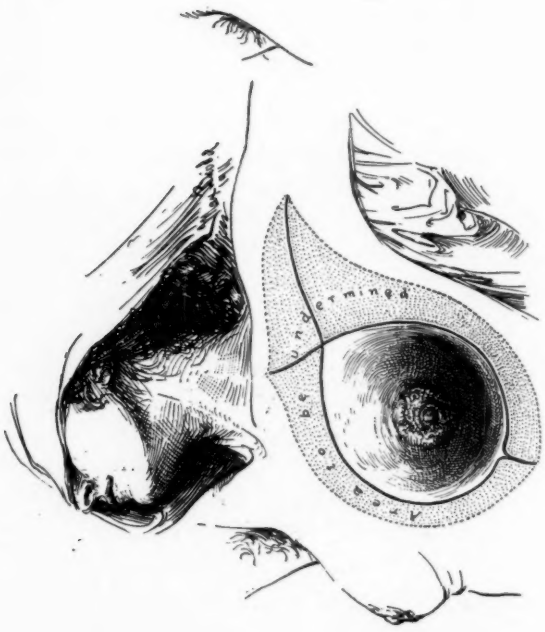
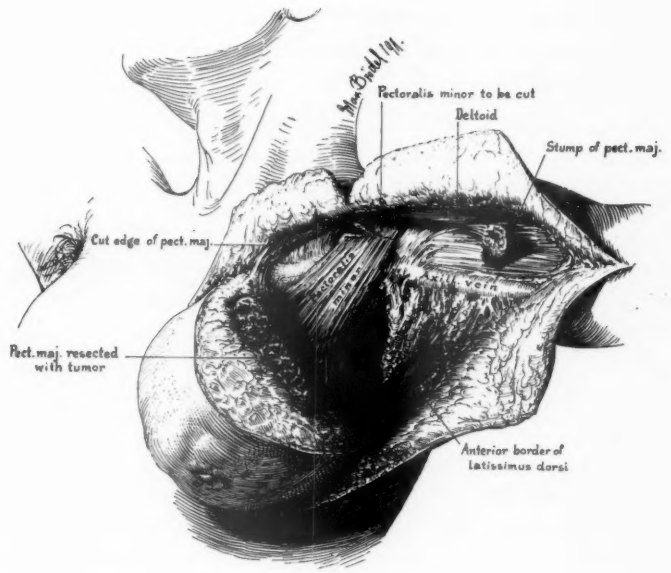


Fig. 9.

Figs. 9 and 10.—Original and hitherto unpublished drawings of the Halsted radical mastectomy by the late Mr. Max Brödel, the distinguished medical illustrator. These drawings were recently discovered in, and loaned from, the early files of the Department of Art as Applied to Medicine of the Johns Hopkins University School of Medicine.

Fust or Fulton; the indisputable inventor.'' Precedence for the modern radical mastectomy is universally bestowed upon William Stewart Halsted—and rightly so. Yet Halsted was certainly not the first to practice removal of the pectoralis major muscle. Celsus cautioned against it almost two thousand years before, and as early as 1570 Barthélemy Cabrol, professor in Montpellier, excised the pectoralis major muscle, dusted the wound with vitriol, and ''cured'' the patient

Fig. 11.



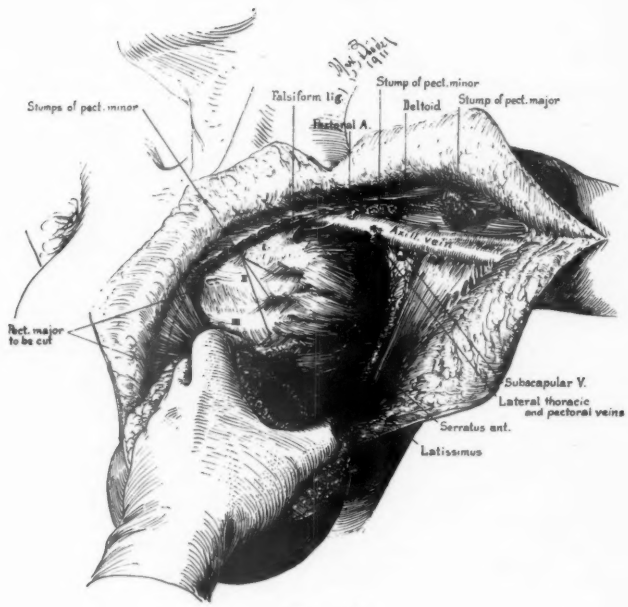


Fig. 12.

Figs. 11 and 12.—Later stages in Halsted's radical operation for breast cancer. Taken from the original drawings which are now on display in the Surgical Library of the Halsted Building of the Johns Hopkins Hospital, used with the permission of the Johns Hopkins Press.

of breast cancer. Petit in France and Volkmann and Heidenhain in Germany both favored and practiced partial removal of the pectoral muscle not infrequently. However, it was Halsted who by scientific surgical study logically conceived of its routine removal as an integral part of the complete operation. He synthesized the best points in the techniques which had been suggested by the most advanced surgeons of the period. It was in the completeness of his method that he achieved a success which set a new standard in the development of breast surgery, and established a paragon of surgical precision which had no precedent in the history of the treatment of malignant disease.

In a beautiful and stirring memorial address, the venerable Dr. Matas had this to say of Dr. Halsted:

> No one who has been privileged to see Dr. Halsted at work on a cancer of the breast, especially during the period between 1895 and 1908, when his publications had attracted many visitors to his clinics to study his methods, could fail to recognize the reason for his extraordinary success. Deeply interested in his work and absorbed in all of its details, whether operating himself or directing his staff of well trained and brilliant assistants, his delicate but far reaching dissections, by which he pursued the disease relentlessly, without regard to esthetic effect or plastic union; his minute and almost fastidious precautions against infection and haemorrhage, controlling the smallest bleeding point so that the total loss of blood throughout the operation was negligible; his skill and nicety in covering large skin defects with autogenic skin grafts in a way that has scarcely been equalled and has never been excelled, and his final dressing of the wound, covering it with silver foil and with immobilizing plaster dressings, gave the impression to the onlooker that he was seeing the performance of an artist close akin to the patient and minute labor of a Venetian or Florentine intaglio cutter or a master worker in mosaic. Yet this task, with all its discipline and method often consumed two and three hours, was practically shockless and bloodless, and was followed almost invariably by recovery.
>
> *Though old the thought and oft exprest,*
> *'Tis his at last who says it best.*

The spirit of Chauvinism burns bright within me, yet in the treatment of cancer tacit allegiance is to men of medicine the world over. Here in the halls of Hopkins our loyalty is to the great Professor and I feel privileged to proudly pay him my humble tribute. Yet in the pageant of history the prime-movers of surgery gradually disappear and fade into an impersonal fusion. The names of such celebrated surgeons as LeDran and Petit of France, Volkmann, Billroth, and Heidenhain in Germany, Moore, Lister, and Banks in England, and Willy Meyer and Halsted in the United States, all indicate that the contemporary pulse of the period was beating in unison throughout the world. The time for radical mastectomy was ripe and its composite character and cosmopolitan development was inevitable.

PRESENT STATUS AND COLLECTIVE REVIEW

Today breast-cancer surgery has again reached a complex state of doubt and dilemma. Haagenson and Stout (1943) have clearly shown that certain advanced cases of breast cancer must be regarded as "categorically inoperable."

Pack (1951) and his courageous colleagues call for total mastectomy—prophylactic bilateral mastectomy for cancer of only one breast. McWhirter, a resolute radiotherapist to the Royal Infirmary of Edinburgh, believes that more lives can be saved in unselected cases by simple mastectomy and superior x-ray therapy. Wangensteen, Urban, Dahl-Iverson, Gordon-Taylor, and Gardner fearlessly explore the mediastinum and neck in an extensive thoracocervical dissection known as the superradical mastectomy. This heroic surgery bordering on "humanectomy" is the contemporary consummation of somatic reduction and "is limited solely by the ability of the human remnant to survive." The leading exponents of radical surgery are seeking "second look" operations, whereas Park and Lees have recently pointed out that it is extremely doubtful that the survival rate of cancer of the breast is influenced by treatment at all, and McKinnon claims that "the failure of early treatment to reduce (breast cancer) mortality shows that spread of remote metastases occurs before interference is possible." Although at the Johns Hopkins Hospital the classic radical mastectomy has provided an over-all ten-year survival for almost 30 per cent of the patients, yet in certain parts of this country breast cancer is still being treated by simple surgery with or without radiotherapy in one-quarter of all such cases.

Considering the duration of life following simple surgery for breast cancer, Sir James Paget (1853) reflected the contemporary opinion of the time when he said, "I am not aware of a single clear instance of recovery—of such recovery, that is, as that the patient should live for more than ten years free from the disease or with the disease stationary." Yet Samuel W. Gross (1880), a disciple of the teachings and principles of Moore (1867), carefully analyzed his own statistics and found about one-sixth of his patients alive and free of disease at the end of ten years. His candid conclusions clearly disclose:

> . . . that when left to itself carcinoma inevitably kills, by its baneful consequences as a local disease, or by its remote multiplication.
>
> That about one in six, or 16.77 per cent, of the patients die of the operation itself; but that the risk is not so great as to forbid interference, since it adds twelve months to the life of the patient.
>
> That thorough operations definitely cure 9.05 per cent of all patients, or more than half as many as it destroys.

The soundest prediction of future progress must come from a realistic view of the past. Only by carefully examining our present precepts and practice can we intelligently plan for the future. Our resolute purpose must always be to promote the best interests of each individual patient, and not those of surgery, radiotherapy, or chemotherapy.

Until a large number of cases of breast cancer are carefully compared by rigorous biostatistical analysis, it is evident that the merit and standard of surgical treatment will remain variable and in doubt. The surgeons of an earlier time who have written treatises on the subject of breast cancer made little attempt to follow their patients carefully. Although some clinicians appear to have been aware of crude survival rates, the postoperative fate of most patients with breast cancer was unknown. The credit for initiating the first systematic

follow-up survey belongs to Volkmann (1875). He subjected all of his operative patients first to a careful microscopic examination with the object of establishing the validity of the diagnosis and then he meticulously traced the patients during their period of postoperative survival.

Lane-Claypon (1924) has reviewed and reported a detailed study of the surgical literature of this early period. Because no standard system of classification and survival reporting had been uniformly adopted—then or now—comparison of results in different countries required an exact scrutiny based upon a precise schedule of analysis.

Conclusions which Lane-Claypon drew from this analysis of early results of approximately 20,000 operative cases of breast cancer (partially listed in Table I) were as follows:

1. After an incomplete or nonradical mastectomy for breast cancer, of a total of 7,029 patients there was a 29.2 per cent three-year survival.
2. After a complete radical mastectomy for breast cancer, of a total of 8,921 patients there was a 43.2 per cent three-year survival.
3. Prognosis following complete operation was greatly affected by the stage of the disease at the time of surgery.

Survival percentage was based upon only those patients successfully followed and did not include those patients considered lost to follow-up. The average five-year survival following radical mastectomy for 2,441 patients traced was 33.1 per cent. The collected results of the complete or radical operation are reported in Table II. All diagnoses were verified by microscopic examination and, as was the custom of the time, all results except those here noted were recorded as three-year survivals.

In an enterprising and unique study of breast cancer as treated in the general hospitals of eight of the largest provincial cities of England and Wales, Lane-Claypon (1928) has analyzed the operative results and survival of 1,642 patients with breast cancer verified by pathologic examination. The years selected for inquiry were 1910 to 1913 and 1919 to 1921, inclusive. The type of operation performed was, of course, of the utmost importance. In all stages of the disease except Stage I the radical operation was performed almost without exception, whereas in Stage I only two-thirds of the patients had a radical mastectomy. The crude survival rates (the proportion of survivors to the total number of patients operated upon without any deletions) were as follows:

	SURVIVAL RATE		
Breast cancer	3 years	5 years	10 years
All stages	50.1 per cent	37.4 per cent	25.2 per cent

However, the difference in survival between the first stage of the disease and the other stages of more advanced breast cancer was enormous. The survival rate for the Stage I cases alone was 85 per cent at three years, 78.5 per cent at five years, and 73.3 per cent at ten years. These over-all results representing radical mastectomy in England for the period 1910 to 1913 and 1919 to 1921 are remarkably good and compare most favorably with present-day surgical accomplishments.

The experience of the Vanderbilt University Hospital has been reported by Brooks and Daniel (1940). During a fourteen-year period prior to 1939, 149 radical mastectomies were performed with only one operative death. However, of seventy-two patients having a high standard of operative technique and having received treatment for a period longer than five years there were twenty-five patients (35.5 per cent) alive and well or "cured" at the end of five years. There were twenty-eight patients (39 per cent) who represented the five-year survival rate if the single patient "dead of other causes" was included as dead of the disease.

Rolf Engelstad (1942) reported the results of treatment at the Norwegian Radium Hospital. Patients observed between the years 1932 and 1937 were treated by radical mastectomy followed by postoperative radium therapy. The absolute five-year symptom-free survival rate (all patients included) was 24.1 per cent of 352 patients. It is to be noted that almost 50 per cent of this group of patients were in Stage IV of the disease at the time of treatment. The special character of this hospital weighs heavily against these statistics.

The records of 3,105 patients with breast cancer treated in nine large American hospitals were reviewed by Hawkins (1944). The status of these patients was presented in terms of the variables of treatment, of the stage and grade of malignancy, and of the host. Five-year survival rates were primarily dependent upon the extent of the disease at the time of treatment. When correction was made for the stage of the disease and type of treatment, all other factors (age, sex, color, and duration of disease) were found to have little or no influence upon survival.

The over-all five-year survival rate (all modes of therapy in all stages of the disease) was 23.9 per cent. Patients who were lost to follow-up were considered dead of the disease although the author points out the difficulty in summarizing these data. The five-year survival rate of patients with Stage I breast cancer was 51 per cent.

The place of surgery and radiotherapy in the management of breast cancer was thoroughly discussed by Richards (1948). Presenting the results of treatment at the Toronto General Hospital during the ten-year period, 1933 to 1943, he noted a marked variation in criteria of operability, surgical technique, and survival time even among the single series of surgeons at this noted hospital. There were 1,189 patients operated upon by thirty surgeons with an over-all five-year survival rate of 43 per cent and a ten-year survival of 26 per cent. All patients were treated by radical mastectomy and postoperative radiotherapy. A plan of future therapy is recommended in which radical surgery is complemented by pre- and postoperative radiotherapy. Patients in the advanced stages of the disease are to be considered primarily within the province of radiotherapy.

In a thoroughly delightful discussion of the treatment of cancer of the breast, Gordon Gordon-Taylor (1948) reminisced regarding his forty years of experience with radical mastectomy. Between December, 1907, and December, 1947, this eminent and eloquent surgeon observed 750 personal patients

TABLE I. EARLY COLLECTIVE REVIEW OF BREAST CANCER AND THE RESULTS OF TREATMENT*

COUNTRY OR TOWN	AUTHOR	DATE	INCOMPLETE				COMPLETE			
			CASES	LOST	SURVIVORS	PER CENT	CASES	LOST	SURVIVORS	PER CENT
Germany										
Berlin (v. Bergmann)	Rotter	1887	109	2	29	27.1	–	–	–	–
	Rotter	1896	–	–	–	–	30	0	11	36.6
	Guleke	1901	704	322	110	28.8	–	–	–	–
Breslau (v. Mikulicz)	Scheu	1907 and earlier	150	23	24	18.9	107	16	18	19.8
Heidelberg	G. B. Schmidt	1889	77	17	17	28.3	–	–	–	–
	Mahler	1900	150	20	35	26.9	–	–	–	–
	Hoffmann	1921	131	0	51	39.0	187	0	65	34.2
Greifswald (Helferich)	Joerss	1897	57	0	13	22.8	35	0	3	8.6
Kiel (v. Esmarck)	Oldekop	1879	173	48	27	21.6	–	–	–	–
	Anschutz and Hellmann	1921	–	–	–	–	235	6	120	52.4
Rostock	Schroeder	1905	347	73	85	31.0	183	7	77	43.7
Stuttgart	Steinthal	1912 and earlier	99	0	27	27.3	101	0	34	33.6
Munich (v. Angerer)	Gebele	1901	203	13	65	34.2	–	–	–	–
	Frankau	1914	49	6	16	36.5	–	–	–	–
Konigsberg (v. Eiselsberg)	Rosenstein	1901	77	26	19	37.3	–	–	–	–
Austria										
Vienna (v. Eiselsberg)	Meissl	1904	181	43	38	27.5	–	–	–	–
	Lazarevic	1914	–	–	–	–	238	100	54	39.1
Vienna (Billroth)	v. Winiwarter	1878	132	35	8	8.3	–	–	–	–
(Hochenegg)	Finsterer	1904	498	164	97	29.0	–	–	–	–
Graz	Schwarz	1905 and earlier	121	0	38	31.4	35	0	8	23.0

*After Lane-Claypon, 1924.

Switzerland										
Zurich	Fischer	1881	54	0	10	18.5	–	–	–	–
Rorschach	Horner	1894	165	7	58	36.7	–	–	–	–
	Wunderli	1906	100	2	22	22.4	–	–	–	–
Norway										
Christiania	Paus	1910 and earlier	6	3	0	0.0	100	27	23	31.5
Italy										
Pisa	Fiori	1909	48	2	27	58.7	24	2	1	4.1
Hungary										
Budapest	Steiner	1906	38	13	4	16.0	22	5	7	41.1
	Dollinger	1908	–	–	–	–	72	11	16	26.2
England										
London	Butlin and Maxwell	1899 and earlier	177	3	32	28.0	48	0	27	56.2
Birmingham (Barling)	Mills	1921	19	0	10	52.6	150	56	46	48.9
Bristol	Morton	1902	39	1	12	31.5	–	–	–	–
	Morton	1922	–	–	–	–	93	30	30	47.6
United States										
New York	Dennis	1891	84	33	27	51.9	–	–	–	–
	Dennis	1907	–	–	–	–	116	0	59	50.8
New York	Pilcher	1894	23	3	7	35.0	–	–	–	–
	Pilcher	1907	–	–	–	–	17	1	9	56.3
Boston	Greenough and others	1907		(some incomplete)			365	0	105	28.9
	Greenough and others	1921	–	–	–	–	69	6	26	41.2
	Cabot	1907	28	0	5	53.5	14	0	7	50.0
Worcester, Mass.	Gage	1905	46	0	11	23.9	–	–	–	–
	Gage and Adams	1911	–	–	–	–	150	1	62	41.6
Rochester, Minn. (Mayo Clinic)	Judd	1914	–	–	–	–	510	85	210	49.4
	Sistrunk and McCarty	1922	–	–	–	–	218	0	113	52.7
Baltimore	Halsted	1907	–	–	–	–	232	18	89	38.3
Total			4,025	859	924	29.2	3,400	371	1,220	40.3

TABLE II. COMPLETE OPERATION. ALL DIAGNOSES SUBJECTED TO MICROSCOPIC EXAMINATION*

NAME AND COUNTRY	EN-TRANTS	DIED UNDER THREE YEARS			LOST	ALIVE AT THREE YEARS
		OF OPER-ATION	OF OTHER CAUSES	OF CANCER		
United States						
Brown	85	0	0	74	0	11
Cabot	14	0	0	7	0	7
Crile	91	0	0	42	4	45
Davis B. Byrom	166	1	0	36	64	65
Deaver and McFarland	200	5	8	45	25	92
Dennis (private)	166	1	0	56	0	59
Gage and Adams	93	2	1	49	1	40
Greenough and others†	365	4	7	249	0	105
Greenough and others	69	0	2	35	6	26
Haggard and Douglass	103	5	0	50	0	48
Halsted	232	4	0	121	18	89
Huntington	13	1	0	10	2	0
Jacobson	71	0	3	33	0	35
Judd	510	0	0	215	85	210
Judd	97	0	0	30	11	0
McCalla	114	0	0	23	0	91
McWilliams	100	4	0	53	26	17
Matas	15	0	2	8	0	0
W. Meyer	84	0	0	40	2	32
Oliver	21	0	0	6	0	15
Peck and White	195	6	0	43	75	50
Primrose (5 years)	45	0	0	25	0	20
Rodman (private)	32	0	0	11	0	21
Sadleir	70	0	5	32	0	28
Sistrunk and McCarty	218	1	0	104	0	113
Vander Veer	103	0	0	17	16	70
Warren	102	0	0	79	0	23
Total	3,324	34	28	1,493	335	1,312
England						
Barker	86	5	0	38	9	29
Watson Cheyne	99	0	1	36	4	31
Handley (private)	52	0	0	27	0	25
Leaf	54	2	0	10	2	40
Leech (private)	11	0	1	2	0	8
Leech (hospital)	88	0	8	37	6	21
Mills (private) 6 years	40	0	0	16	9	15
Mills (hospital) 3 years	110	0	0	32	47	31
Monsarrat	36	0	2	8	0	31
Morton‡	93	6	0	27	30	30
Rigby (private)	16	0	0	2	1	4
Rigby (hospital)	62	0	0	14	12	5
Sheild	60	2	0	12	1	21
Total	807	15	12	261	121	286
Germany						
Boss	127	0	0	58	18	51
Hoffmann	187	0	0	119	0	68
Joerss	36	0	1	24	1	10
Lindenburg	183	13	5	81	7	77
Neher	362	16	17	158	7	96
Rosenstein	68	2	0	17	9	1
Salomon	86	1	0	56	0	29
Scheu	107	0	0	73	16	18
Steinthal	101	5	10	52	0	34
Tietze	54	1	0	33	7	13
Total	1,311	38	33	671	65	397
France						
Begouin	133	0	6 (cause? in 20 cases)	51	38	27
Berard	185	0	0	55	98	32
Delbet	100	0	3	9	72	16
Forgue	285	0	0	170	0	115
Hartmann and Bergeret	328	0	0	120	80	106
Grenade	106	2	4	30	17	53

*After Lane-Claypon, 1924.

†86 incomplete not separable.

‡Some patients recorded among "lost" cases were almost certainly alive.

TABLE II—CONT'D

NAME AND COUNTRY	EN-TRANTS	DIED UNDER THREE YEARS			LOST	ALIVE AT THREE YEARS
		OF OPER-(TION	OF OTHER CAUSES	OF CANCER		
Heurtaux (4 years)	341	14	17	110	61	139
Lapeyre	225	0	0	26	61	138
Le Dentu	59	0	0	25	0	34
Walther (private)	81	0	0	20	16	38
Walther (hospital)	37	0	0	12	0	25
Total	1,880	16	30	628	443	723
Austria						
Lazarievie	238	4	4	76	100	54
Schwarz	51	3	1	23	0	8
Schwarzkopf	31	3	0	13	6	3
Total	320	10	5	112	106	65
Hungary						
Dollinger	72	3	0	42	11	16
Steiner	22	1	0	9	5	7
Total	94	4	0	51	16	23
Switzerland						
Meyer (Kocher)	212	0	0	146	0	66
Wiesmann	93	0	0	54	0	39
Wunderli	52	0	0	26	0	11
Total	357	0	0	226	0	116
Italy						
Fiori	23	0	0	20	2	1
Sweden						
Borelius	84	1	0	48	6	29
Brattstrom	295	0	0	136	39	120
Total	379	1	0	184	45	149
Norway						
Paus	100	1	2	47	27	23
Holst (private)	19	0	1	10	0	8
Holst (hospital)	44	0	2	30	3	9
Total	163	1	5	87	30	40
Holland						
Deelman	391	0	0	180	91	120
Kropfeld	56	0	5	24	0	27
Total	447	0	5	204	91	147
Total all countries	9,105	119	118	3,937	1,254	3,259

with primary breast cancer. Of this total number only 645 patients were treated by radical mastectomy, the remainder being subject to such clinical selectivity which favored simple surgery or radiotherapy.

Using the "ambitious yardstick" of only a ten-year survival rate Gordon-Taylor reported 43 per cent of 388 patients (all operated upon prior to 1929) alive at the end of ten years following radical mastectomy. There were 113 patients with Stage I breast cancer in whom the ten-year survival rate was 84 per cent; there were 204 patients with Stage II breast cancer in whom the ten-year survival rate was 29.4 per cent; and there were forty-six patients with Stage II breast cancer in whom the ten-year survival rate was 6.5 per cent.

These extraordinary survival statistics are the story of one surgeon's experience dealing "with what might be regarded as a relatively favourable class of case." Commenting upon the noteworthy survival rate of this master surgeon, an English colleague has been heard to remark that a woman is better off with Stage I breast cancer in the hands of Gordon-Taylor than if she were perfectly normal and living out her London life expectancy.

The surgical problems involved in breast cancer were ably discussed by Adair in his Moynihan Lecture delivered before the Royal College of Surgeons in 1949. The vast array of clinical material at his disposal at the Memorial Hospital is incomparable. "Our experience, philosophy and conclusions are based on the care and study of 13,054 cases of breast cancer at the Memorial Hospital." Adair notes that there are few fields in medicine or science where there is a greater uncertainty in evaluating therapy than in the biostatistics of breast cancer. "The method by which some investigators arrive at the statistical results of therapy is quite different from that of another group, making it so that comparisons are impossible." Criteria of operability are also highly flexible, and an enthusiastic surgeon may find this borderline a broad and challenging frontier: "they make a glorious shipwreck who are lost in seeking worlds" beyond their reach. Operability, according to Adair, is interpreted along "very generous standards" at the Memorial Hospital. Yet, despite this liberal selection of patients, the over-all survival rate in 3,988 cases (1935 to 1942), including every case, advanced as well as operable, was remarkably good, 39.6 per cent.

Consideration of the operable material for the years 1940 to 1942 indicates that the five-year survivals in cases treated by radical mastectomy were as follows:

	PER CENT
All primary operable cases	58.3
Breast alone involved	82.2
Breast and axilla involved	43.5

Postoperative x-ray therapy following radical mastectomy was administered only in those cases in which patients had axillary involvement. It should be noted, however, that these statistics are exclusive of an "indeterminate group" which included among others patients who were lost to follow-up and patients who died of intercurrent disease within five years. The excellent end results are indeed a tribute to the skill and ability of Adair.

At the Radiumhemmet in Stockholm, Berven (1949) has reviewed 3,623 cases of breast cancer observed during the period 1921 to 1941. These cases consisted of the following groups: (1) 1,164 patients having pre- and postoperative radiotherapy, (2) 640 patients having postoperative radiotherapy, (3) 535 patients with recurrences following surgery elsewhere, (4) 544 patients having palliative radiotherapy, (5) 740 patients having no treatment.

During the period 1921 to 1935 there were 1,035 patients treated by radical surgery and radiotherapy with a five-year survival rate of 46 per cent and a five-year "cure" rate of 42 per cent. In the period 1936 to 1941 there were 769 patients treated similarly with a five-year survival rate of 51 per cent and a

five-year "cure" rate of 43 per cent. There appeared to be no difference in the survival rate between patients treated with both pre- and postoperative irradiation and those treated with only postoperative irradiation.

Windeyer (1949) has recently reported the results of breast cancer treatment at the Middlesex Hospital during the years 1936 to 1942. Of a total number of 1,091 patients who applied for treatment, 977 were primary patients who had had no previous treatment and 114 were secondary patients who had received surgical treatment elsewhere. Of the remaining 977 patients, sixty received no treatment whatsoever because of either refusal or advanced disease. Follow-up has been excellent (97.4 per cent), and all patients untraced were considered as having died of cancer.

Treatment was variable but in general consisted of radical mastectomy in Stage I, radical mastectomy followed by postoperative radiotherapy in Stage II, and radiotherapy with or without simple surgery in Stages III and IV.

The over-all five-year survival rate of 917 patients was 34 per cent and the ten-year survival rate was 21.9 per cent. In a selected group of "operable" patients treated by radical mastectomy the corrected five-year survival rate was 42.9 per cent and the ten-year survival rate was 29 per cent. These statistics, which are representative of one of London's great teaching hospitals, closely correspond to those of Lewison, Trimble, and Griffith reporting their results from the Johns Hopkins Hospital of Baltimore.

In an excellent clinical study of 1,042 cases of breast cancer treated at the Radiumhemmet, Nohrman (1949) reported the end results of treatment for the period 1936 to 1941. Of these patients, 997 were accepted for treatment and 0.9 per cent were men. Twenty per cent of the series were considered inoperable. Although radical mastectomy was performed in the remaining 767 patients the results of treatment were also computed for an unselected group of 660 patients.

The absolute five-year survival rate (all patients treated and untreated) was 40.1 per cent. The five-year survival rate following radical mastectomy was 50.6 per cent for the entire group and 54.7 per cent for the unselected group. Preoperative irradiation appeared to have improved the end results in the most unfavorable patients, whereas in the remaining patients no significant difference could be demonstrated between the results of treatment with combined pre- and postoperative irradiation and with postoperative irradiation alone.

The results of radical mastectomy in the treatment of cancer of the breast at the Massachusetts General Hospital have recently been reported by Taylor and Wallace (1950). The five-year over-all "cure" rate for the period 1936 to 1941 was 51 per cent. In 169 cases the axilla was not involved and the five-year "cure" rate was 77 per cent, and in 261 cases the axilla was involved and the five-year "cure" rate was 33 per cent. In computing the "cure" rate, all patients submitted to surgery were included, except those known to have died of intercurrent disease (without evidence of recurrence) in less than five years after operation. Untraced patients and patients with recurrent disease were included but classed as failures. Thus, "cured" patients were those known to

be living and free from disease five years following surgery, in addition to those dying without recurrence after five years. These definitions must be clearly kept in mind in comparing survival rates between clinics. However, during the past fifty years there has been a definite and continuous improvement in the results of radical mastectomy at the Massachusetts General Hospital.

Haagensen and Stout (1951) have again carefully reviewed the results of radical mastectomy at the Presbyterian Hospital between the years 1935 and 1942, inclusive. Strict and specific criteria of operability which have been published previously guided their selection of cases for radical mastectomy. The fidelity of follow-up was exceedingly good, 96.2 per cent of all patients being followed for five years or until death. Computation was based upon both relative and absolute five-year clinical "cure" and five-year survival rates. In the analysis of the relative "cure" rates no deductions have been made from the total number of primary cases in which treatment was started. Patients dying of unknown cause or of intercurrent disease, or lost to follow-up before the end of the five-year period, were considered dead of breast cancer. Absolute "cure" and survival rates were based upon all patients with primary breast cancer coming to the Presbyterian Hospital.

The five-year end results of radical mastectomy were as follows:

	NUMBER	PER CENT
1. Radical mastectomies	495	
2. Operative deaths	9	1.8
3. Lost to follow-up	19	3.8
4. Died of unknown cause before 5 years	7	1.4
5. Died of intercurrent disease before 5 years	18	3.6
6. Died of breast cancer before 5 years	154	31.1
7. Alive, with recurrence at 5 years	47	9.5
8. Alive, without recurrence at 5 years	241	48.7

Thus, the relative five-year clinical "cure" rate (without deductions) was 48.7 per cent, and the relative five-year survival rate was 58.2 per cent. These results represent an improvement of 10 to 15 per cent over the relative rates reported for the years 1915 to 1934.

In this series of critically analyzed cases there were 668 female patients with primary breast cancer who applied for treatment. Only 495 received a radical mastectomy, the remainder either being treated by simple surgery, x-ray therapy, or not being treated at all. The absolute five-year survival rate (total number of survivors divided by the total number of primary patients) was 47.2 per cent, and the absolute five-year "cure" rate was 38.6 per cent. The diligent care and exactitude of Haagensen's statistics reflect the merit of his enterprise in the study of breast disease.

A review of all patients with cancer of the breast recorded at the University of California Hospital and Clinics during the thirty-year period 1918 to 1947, inclusive, was analyzed and recently reported by Shimkin, Lucia, Stone, and Bell (1952). The clinical material consisted of 1,056 female patients of whom 94 per cent had pathologic verification of breast cancer, and 98.5 per cent were successfully followed for at least five years.

The five-year survival rate of all patients, 68 per cent of whom already had metastases (Stages II, III, or IV) at the time of admission or operation, and including all untreated and untraced patients, was 40.4 per cent. The five-year survival rate following surgery was 72.5 per cent for all Stage I patients, 42.2 per cent for all stage II patients, 18.4 per cent for all Stage III patients with extensive axillary and local disease, and there were no survivors among Stage IV patients. Significant differences in survival were considered to be "dependent upon anatomical extent of the disease at the time of treatment, which is determined primarily by the biologic properties of the neoplasm and possible host-resistance factors, and by the delay from apparent onset to treatment."

In a carefully computed and rigorously analyzed study of 1,777 new patients with breast cancer seen at the Royal Cancer Hospital, Smithers, Rigby-Jones, Galton, and Payne (1952) reported the results of treatment from 1937 to 1948, inclusive. The absolute five-year survival rate of all new patients, men and women, treated and untreated, was 34.6 per cent. All patients lost to follow-up were considered dead of the disease, and treatment consisted of both radical mastectomy and/or radiotherapy. The absolute ten-year survival rate was 21 per cent. The net five-year survival (excluding those patients lost to follow-up and those having died of intercurrent disease) was 40 per cent.

At the Mayo Clinic, Harrington (1952) has reported the results of surgical treatment of unilateral breast cancer in women for the period 1910 to 1946, inclusive. Treatment consisted of radical mastectomy followed by radiotherapy in patients with malignant axillary nodes. Follow-up study was successful in 98.4 per cent of the patients; however, those patients lost to follow-up were dropped from the study and excluded from statistical analysis. All patients known to have died were considered dead of the disease. Only those patients treated by radical mastectomy were reviewed. The survival rate was recorded as follows:

VERIFIED AXILLARY METASTASES	SURVIVAL RATE (PER CENT)	
	5 YEARS POSTOPERATIVELY	10 YEARS POSTOPERATIVELY
Present	32.5	18.0
Absent	78.3	61.2
Total	51.2	34.6

A quinquennial study during this period indicated a consistent and progressive improvement obtained by radical mastectomy during the course of these many years. Criteria of operability have always been quite lenient, and a change in these criteria could hardly account for the appreciable increase in the survival rate. Earlier diagnosis and more effective treatment must certainly play a responsible role.

In discussing the results of radical mastectomy, Halsted (1907) asserted that in the ultimate survival of the patient "the variety of the cancer, the

time elapsed since its appearance, the degree of outlying involvement, the activity of the gland (lactation, age of the patient), the thoroughness of the operation, are important factors.'' The results of radical operations for the cure of cancer of the breast at the Johns Hopkins Hospital were reported by Halsted in 1907. Excluding sixty-five patients in whom simple surgery was found more suitable, there remained 232 patients treated by radical mastectomy. In about one-half the patients a supraclavicular neck dissection was combined with radical mastectomy. The end results in eighteen patients were unknown; nevertheless, these untraced patients were computed as dead of the disease.

The three-year survival rate was 38.3 per cent with a relative ''cure'' rate of 32.3 per cent. The five-year survival rate was 28.9 per cent with a relative ''cure'' rate of 24 per cent.

Lewis and Rienhoff (1932) in a most exhaustive study reviewed a series of 950 consecutive breast-cancer cases observed at the Johns Hopkins Hospital during the forty-two-year period 1889 to 1931. It is unfortunate but readily understandable that during this long time-lag in follow-up 22 per cent of the patients were completely untraced. Consequently, because of this and other factors, of an over-all total of 950 patients, accurate survival information (known dead) was available in only 420 or 44.2 per cent. Considering only these 420 patients the five-year survival following radical surgery was 18.1 per cent. At the time of the Lewis and Rienhoff report there were 97 patients living and well of whom 67 per cent had survived five years.

An analysis of the results of treatment at the Johns Hopkins Hospital for the eleven-year period 1932-1942 was carefully reported by Jones (1949). Beginning in 1932 there were 304 ward patients (private patients were not included in this study) admitted to the wards of the hospital during this period. Fifty-two (17 per cent) of these patients were considered unsuitable for radical mastectomy and were treated by radiotherapy with or without simple surgery. There were thirty-one patients (12 per cent) lost to follow-up.

The over-all five-year survival rate (excluding those patients lost to follow-up) was 34 per cent. Considering all patients lost to follow-up as having died of cancer, the corrected five-year survival rate would then become 29.3 per cent, a figure almost identical with the earlier results of Halsted. The five-year survival rate for patients with negative axillary nodes by pathologic examination was 66 per cent, whereas it was only 26 per cent in patients with axillary metastases.

Lewison, Trimble and Griffith (in press) reviewing the latest results of treatment at the Johns Hopkins Hospital report the five- and ten-year survival rates for all patients treated by surgery during the period 1935 to 1940, inclusive. Successful follow-up was achieved in 95 per cent of 220 patients. Radical mastectomy with or without radiotherapy was performed in 204 patients. Simple mastectomy was performed in fourteen patients, and local ex-

cision was performed in two patients (one patient refusing further surgery and the other having extensive pulmonary metastases). All cases were verified by pathologic examination and patients lost to follow-up and dead of intercurrent disease were considered as dead of cancer.

For all cases of breast cancer treated by surgery the five-year survival rate was 43.2 per cent, whereas the five-year "cure" rate was 38.2 per cent. These figures represent an improvement in end results of almost 15 per cent above the earliest Johns Hopkins Hospital survival statistics reported by Halsted almost fifty years ago.

The technique of radical breast surgery as performed at the Johns Hopkins Hospital and its indications have been described by Trimble (1940). Such important problems as pre- or postoperative radiotherapy, castration, and the question of simple mastectomy are analyzed and discussed. The extent to which radiotherapy should augment surgery remains indecisive even among those with considerable experience. Sprong and Pollock (1951) have reviewed the rationale of radical mastectomy from a similar point of view.

Geschickter in his excellent book entitled *Diseases of the Breast* (1948) has analyzed the five-year survival rate of 1,957 patients with breast cancer. It is presumed that some of this clinical material represents patients treated at the Johns Hopkins Hospital prior to 1942. This series included seventy-five patients in whom no treatment was given. The rate of successful follow-up was not stated. The over-all five-year survival rate was 34.1 per cent. Patients without axillary metastases had a five-year survival rate of 66 per cent, and patients with axillary metastases had a five-year survival rate of 19 per cent.

In a comparative review of treatment in the American literature Geschickter found an average five-year survival rate of 36.9 per cent. This clinical material represented a total of 8,585 cases of breast cancer reported by thirteen different groups of surgeons. Patients without axillary metastases had a five-year survival rate of 66.7 per cent, and patients with axillary metastases had a five-year survival rate of 23 per cent.

A unique and interesting study of 298 consecutive cases of breast cancer was reported by Finney, Merkel, and Miller (1947). All cases were those of the private patients of four exceptionally prominent and superior surgeons who received their training either directly or indirectly from Dr. William S. Halsted.

The fifteen-year period 1930 to 1945 was analyzed, and the diagnosis was confirmed by microscopic examination in every case. All patients were treated by radical mastectomy with supplementary radiotherapy being given to only nineteen patients. Follow-up was exceedingly good, being successful in 280 patients (94 per cent). The operative mortality was low, three patients (1 per cent) dying as the result of surgery.

The five-year survival rate (calculated exclusive of those patients lost to follow-up and postoperative deaths) was 49 per cent. The ten-year survival rate was 19 per cent. When the over-all survival rate is corrected to include total patients treated, there was a five-year survival rate of 45.3 per cent and a ten-year survival rate of 17.4 per cent.

In a provocative and candid but controversial study of the treatment of breast cancer by simple mastectomy combined with a high standard of radiotherapy, McWhirter (1950) harks back to the suggestions of Borak (1936), Grace (1937), Mitchiner, Bailey, and Price (1937), Erskine (1935) and many continental surgeons of this and an earlier day in what some critics call a pirouette of history repeating itself. The contentions of McWhirter are based upon the obvious fact that the majority of patients with breast cancer are first seen when cancer is no longer confined to the breast alone. Without exception there is universal accord that the results of radical mastectomy are excellent so long as the disease remains confined to the breast; however, as soon as the axilla becomes involved the results become considerably less favorable. Therefore, since surgical excision of the axilla is unnecessary when these regional nodes are innocent, and radical mastectomy so often fails when these nodes are contaminated, McWhirter has advocated simple mastectomy followed by carefully planned radiotherapy in an extensive trial for patients with breast cancer. This method of combined treatment is recommended as suitable for a large proportion of the total number of patients who are routinely seen with breast cancer. Simple mastectomy alone has not been designed or recommended to replace radical mastectomy.

TABLE III. A REVIEW OF ALL PATIENTS WITH BREAST CANCER (1,345) OBSERVED BY McWHIRTER (1941 TO 1945)*

OPERABLE, 60 PER CENT		INOPERABLE (RADICAL OPERATION), 40 PER CENT	
AXILLARY GLANDS NEGATIVE	AXILLARY GLANDS POSITIVE	ADVANCED LOCALLY	DISTANT METASTASES
24 per cent	36 per cent	25 per cent	15 per cent
Axillary dissection unnecessary	Disputed group	Radical mastectomy contraindicated	Radical mastectomy contraindicated
Simple mastectomy + x-rays	Simple mastectomy + x-rays	Simple mastectomy + x-rays or x-rays alone	No treatment or palliative treatment
5 year survival rate, 89 per cent	5 year survival rate, 44 per cent		
All operable patients (757), 5 year survival rate, 62 per cent		All patients with locally advanced cancer (389), 5 year survival rate, 29 per cent	
All patients without evidence of distant metastases (1,146), 5 year survival rate, 50.5 per cent			
Every patient (treated and untreated) coming to the hospital (1,345), 5 year survival rate, 43.7 per cent			

*After McWhirter, 1950.

Five main principles in the radiotherapy of breast cancer are emphasized: (1) The axillary and supraclavicular nodes must be treated as one continuous chain. (2) The internal mammary nodes must be treated in continuity with the chest wall. (3) Hard quality radiation is essential. (4) Adequate dosage must be delivered throughout the entire area of treatment. (5) Only one course of treatment should be given.

In Edinburgh the policy adopted has been to carry out only a simple mastectomy and to treat the axilla entirely by radiotherapy. The results of all cases (1,345) referred from almost all of South and East Scotland between the years 1941 and 1945 are shown in Table III.

The five-year survival of all patients coming to the hospital (treated and untreated) was 43.7 per cent. There certainly appears to be no marked or significant difference between this survival rate and the over-all survival rate of 39.6 per cent at Memorial Hospital, of 47.2 per cent at Presbyterian Hospital, or of the survival rate at similar superior surgical clinics. Careful study of McWhirter's statistics indicates (assuming his "operable" cases to be comparable to Stage I and Stage II) a five-year survival rate of 62 per cent; and a five-year survival rate of 50.5 per cent if one includes all cases without evidence of distant metastases.

Although the prejudices of doubt are difficult to destroy, it is clearly evident that the five-year survival rates reported by McWhirter are equal to any achieved by the accepted procedure of a classic Halsted radical mastectomy, with or without radiotherapy. It is, of course, quite obvious that the principles of McWhirter are not merely simple mastectomy and intensive radiotherapy. Special techniques are employed both at operation and in the administration of x-ray therapy.

If one could reduce the margin of clinical diagnostic error to a minimum, then all patients with Stage I breast cancer could be safely and successfully treated by simple mastectomy. However, the thorns of experience have taught us that diagnostic errors based upon physical examination alone may vary between 25 and 50 per cent. Thus, the hazards of planning a treatment policy based upon the clinical diagnostic staging of the disease are evident.

The success of the McWhirter technique lies primarily in the very early and late cases of breast cancer. In the middle group of borderline cases with less extensive axillary involvement, confidence in well-planned radical surgery of the axilla must merit our continued trust. Regardless of McWhirter's most gratifying survival statistics, sceptics and sound surgeons as well still believe the surest and safest method of eradicating axillary metastases is by radical surgical excision. Time alone will tell—and when the ten-year survival rate is disclosed perhaps the added "years teach much which the days never know." However, in the early light of McWhirter's statistics the logic of radical mastectomy may rest upon reasons which reason alone finds difficult to define. By his renaissance of an idea which had long since lapsed into

the limbo of the past, McWhirter challenges our current complacency. Future experience alone must be the immutable standard of impartial judgment.

Keynes (1952), a staunch advocate of conservative surgery and radiotherapy, observes that "orthodoxy has been greatly shocked by this subversive tendency . . . but history cannot be denied." Unfurled prophecy, however, must not be confused with either history or destiny.

Sir Heneage Ogilvie has published the final pages of a diary which he kept during a visit to America in 1937. The heterodox Sir Heneage had this to say concerning the orthodox Halsted tradition:

> I watched several dyed-in-the-wool Halstedians performing the radical amputation of the breast, and I felt that here the knife ideal, carried to its extreme, is the "letter that killeth." A dissection of the axilla with the knife is distressing to watch; the surgeon takes more than an hour to do part of the operation for which we should need ten minutes . . . .

W. Sampson Handley (1927) was one of the first to call attention to the frequency of internal mammary lymph-node metastases in breast cancer, and he advocated the parasternal insertion of radon as an operative precaution. The excellent work of Richard S. Handley (1952) has recently extended the original investigations of his eminent father. In a series of 119 patients with operable breast cancer Handley biopsied the internal mammary lymph nodes as a sort of "pathologic reconnaissance." In 34 per cent of these cases metastases had already invaded the internal mammary chain of nodes, and presumably radical mastectomy in these cases was doomed before it was begun. In discussing the practical implications of these findings the speculations of Handley are particularly pertinent. Readily admitting that the axillary lymphatic pathways are the main drainage channel of the breast, Handley contends that:

> The case is far otherwise with the internal mammary chain. It lies on the pleura and is a main lymphatic road from the liver and diaphragm. It is very difficult to reach surgically, yet is often heavily implicated. Not only do I think that spread of carcinoma to the internal mammary chain accounts for those puzzling recurrences which occur when a radical mastectomy has been done on an early case, but I also believe that it accounts for the fact that metastasis is commonest in the lungs and pleura and that, in post-mortem series, the liver is the second most commonly invaded organ. I think in fact, that in breast carcinoma, the internal mammary chain is the principle highway of death.

In the light of these important findings a small group of surgeons have renewed their efforts to increase the scope of the classic Halsted radical mastectomy. Among these champions of superradical mastectomy, Wangensteen has noted that approximately 60 per cent of patients having cancer of the breast with axillary involvement have evidence of the disease beyond the reach of the conventional radical mastectomy. These metastases have been noted in the internal mammary chain of lymph nodes, in the mediastinal lymph nodes, and in the supraclavicular region. By means of a cervicothoracic ap-

proach and median sternotomy, the classic radical mastectomy has been extended by Wangensteen to include a supraclavicular dissection, an upper mediastinal dissection, and removal of the internal mammary chain of lymph nodes. The mortality and morbidity associated with this type of heroic surgery remain to be formally reported in the medical literature, whereas survival must await the test of time.

Wangensteen, who is a distinguished surgeon and careful critic, states that, "Today it should be said, I believe, the Halsted operation for cancer of the breast is outmoded: it is not radical enough; it is an incomplete operation for cancer of the breast in patients exhibiting axillary metastases." However, there are those who believe that the strength of this criticism does not "lie in the weakness of the thing criticised." For to criticize an operation is certainly easier than to improve one. It remains to be seen whether such strategic surgery as superradical mastectomy can more successfully cope with breast cancer which has already spread to the internal mammary nodes on the same side and probably beyond.

Gardner has combined supraclavicular and internal mammary node dissection with radical mastectomy in a small number of patients. Andreassen[99] and Dahl-Iversen have performed prophylactic supraclavicular dissection combined with radical mastectomy and found malignant nodes in 17 per cent of their cases.

In a recent report Urban discusses his experience at the Memorial Hospital in New York where he treated fifty-seven patients with primary operable breast cancer by removing the internal mammary lymph node chain en bloc in continuity with a portion of the anterior chest wall and radical mastectomy. This formidable operation is recommended particularly for Stage I and early Stage II lesions, especially when these are located in the medial quadrants. In the skilled hands of this surgeon there has been no mortality and little increase in postoperative morbidity, although one patient "died two days postoperatively from a cerebral vascular thrombosis after an apparently normal recovery from surgery." Invalidism has been minimal and long-term end results are, of course, as yet unknown, but it is encouraging to note a complete absence of local recurrences in a short period of time.

There are few fields with more pitfalls for the statistically unwary than the coding of cancer and computation of the end results of cancer therapy. Almost fifty years ago Halsted commented that "it is especially true of mammary cancer that the surgeon interested in furnishing the best statistics may in perfectly honorable ways provide them. The most conscientious man may refuse to operate upon any but favorable cases . . . ." Today national and international cancer societies are urging uniformity and standardization in reporting cancer statistics. The following code for the clinical staging of accessible tumors recommended by the American Cancer Society and the International Union Against Cancer is a major move in the elimination of the "built-in-bias" in cancer biostatistics:

CODING OF BREAST CANCER BY STAGES

Primary site:

0 No tumor.

I Tumor infiltrating the primary organ site.

II Tumor of relatively larger size, infiltrating the primary organ site and not extending beyond the adjacent soft tissues.

III Tumor widely infiltrating primary organ site and extending to neighboring organs.

IV Tumor extensively involving adjacent soft tissues or organs.

Metastases:

0 None.

I Regional lymph nodes slightly enlarged, discrete, and movable.

II Regional lymph nodes considerably enlarged, and fixed either to one another or to adjacent structures.

A Clinical stages confirmed microscopically.

It is, of course, desirable that criteria for determining the clinical stages of breast cancer should be based upon physical examination supplemented by simple instrumentation available to all physicians.

Real benefit can be derived from a review of the end results of treatment only if a great deal of scrupulous care and strict uniformity in recording and presenting clinical material is rigorously observed. It is necessary to present all of our results so that they will be forthright and intelligible to others, comparable with similar studies the world over, and indicative of genuine improvement over alternative modes of treatment or even over the natural life expectancy if no treatment is given at all. The wisdom of White (1951) is clearly evident by his sound perception of this very problem. The validity of comparative results must be based upon a common language applicable to the type of disease, operative procedure, selection of cases, and uniformity of the reports. Decisive factors other than treatment do, of course, influence survival and prognosis in cases of breast cancer. Important antecedent factors (heredity, fertility, age, marital status, pregnancy, and lactation history), grading the degree of malignancy, tumor size, position and rate of growth, staging of the disease, host resistance, duration of the disease, selection of patients, and criteria of operability present many difficulties in classification which must be successfully solved before determining the best treatment for each patient.

> As noted by Smithers and his colleagues: . . . comparisons of overall results obtained in the best treatment centres which do provide the basic data on which absolute survival-rates can be calculated show that a steady improvement has occurred over the years but do not yet provide conclusive evidence that the slight differences observed in groups treated at about the same time are due to the treatment methods advocated and not to variations in the material treated.

Perhaps it is not entirely a mirage of hope to predict that future methods of cancer therapy will probably improve. Supervoltage radiotherapy and the clinical application of isotopes will surely find an ever-increasing field of use-

fulness, but it is doubtful whether these innovations will be spectacular. Refinements in the technique of radical mastectomy or superradical mastectomy, even when performed promptly, meticulously, and with the utmost of skill, can hardly be the ultimate answer. The anatomic limit of free franchise among competent breast surgeons remains to be expediently defined. Time alone will properly evaluate the place of conservative or ultraradical breast surgery, but until then they should be cautiously undertaken as a clinico-experimental exercise and performed in a spirit of hopeful consideration, for "when desperate ills demand a cure, distrust is cowardice and prudence a folly." The urgent need for an effective cancer chemotherapeutic agent, a selective cell poison, an antimetabolite against cancer, an adjunct to host resistance, a tumor-inhibiting steroid, or antiviral antibiotic can best be measured by today's appalling toll of cancer of the breast. However, this universal faith in an inevitable cancer "cure" still remains the triumph of hope over clinical experience. In his 1952 presidential address before the American Association for Cancer Research, Steiner estimated the total number of cases of cancer in the United States alone for the year 1948 to be 286,721, with cancer of the breast representing about 10 per cent of all cases. American Cancer Society statistics indicate that one woman in twenty-five who reaches adult life is destined to develop breast cancer.

The glorious goal in the "cure" of breast cancer is the removal of the primary tumor with *all* of its areas of lymph drainage. This, of course, must be done before the disease has disseminated (by both blood and lymph channels) beyond the scope of surgery. It is a matter of the greatest importance, as suggested by Stone, to determine the limitations wherein the increased salvage of extended radical mastectomy is offset by the law of diminishing returns (increased operative mortality, morbidity, and postoperative disability). The interception of such crucial avenues of death as blood-borne metastases, mediastinal, pleural, supraclavicular, and contralateral axillary and internal mammary lymph node metastases remain without serious interdiction despite the strategy of superradical surgery.

Thus, the fundamental principles of radical mastectomy in the surgical treatment of breast cancer must not be abandoned as untenable in favor of either more formidable or more conservative procedures. Despite the admonitions of contemporary Cassandras, the classic Halsted radical mastectomy is by no means obsolete. It remains a rampart of preservation and is the operation of choice in most cases of cancer of the breast.

However, current concepts of breast cancer are constantly changing. The idea of a single focus of malignant growth is gradually giving way before the theory of multicentric origin. The prophecy of recent experience throws new light on the curious pattern of breast cancer behavior—during pregnancy, at the menopause, following castration, during the administration of the sex steroids, and subsequent to adrenal ablation. The concept of the complete autonomy of the breast cancer cell is no longer sacred. Even the subtle in-

fluence of an upset hormone homeostasis can modify the course of malignancy. The perplexing pattern of the distribution of metastases—frequent in the bones of the spine and pelvis, infrequent in the bones below the knee or elbow, common in the visceral organs, uncommon in the skeletal muscle—remains an oft observed fact in this disease while its explanation remains knowledge deferred. Although observation and logic are said to be the beacons of wisdom, yet science is disillusioned in seeking the reason for a nidus of breast cancer cells lying dormant for twenty, thirty, or even forty years before becoming a fulminating harbinger of death. Why are the results of radical treatment in advanced breast cancer so much worse than simple surgery, x-ray therapy, hormone therapy, or even no treatment at all? What are the basic principles of stromal-tumor-host relationships?

In a distinguished paper, Smithers suggests that perhaps future progress in the treatment of breast cancer may depend upon our accepting the present uncertainty of tumor behavior, prodding ourselves out of the belief that what we know how to do best by training and tradition must of necessity be best for our patients and that any improvement in results is due to our own operative effort. Simple surgery, improved radiotherapy, and hormone administration in selected cases may be of considerable importance in allowing a patient to live out her normal life span in comfort. A careful study of each patient to assess the degree of advancement of the disease as well as the pain and suffering, both mental and physical, should aid us in our therapeutic aim, thus achieving the best treatment policy for each individual patient. In this light the epitaph of Trudeau takes on a special meaning: "To cure sometimes, to relieve often, to comfort always."

It is, of course, obvious that there are many problems relating to the surgical treatment of breast cancer which have yet to be solved. In an excellent evaluation of this subject Orr (1950) reminds us that "to champion one method of treatment or technique of operation to the exclusion of all others may smack of dogmatism, and dogmatism never does much toward the solving of scientific problems. . . . We must keep an open and discriminating mind concerning the many opinions extant, and look with a discerning eye upon future conclusions which may lack basic truths. Opinions should be respected, but should not be mistaken for facts."

CONCLUSIONS

Breast cancer is an ancient and elusive disease which has claimed its many victims in all walks of life at almost every age and from time immemorial. Generation after rising generation of physicians and surgeons has challenged this dread disease, resorting to every therapeutic regimen considered curative at the time. It seems strange indeed that, despite the tremendous strides of our healing art, cancer mortality has not yet reflected to any major degree the scientific solace of the wonder drugs or the bountiful benefits of an ever-improving surgical skill. Nevertheless, living in an age of modern medical

miracles we may rightly hope that this malignancy, like many sinister scourges, may be ultimately conquered. Until then, however, we must strive to increase our current treasury of knowledge and by our present practice provide the best possible treatment for each individual patient.

The ancient Roman Seneca once said, "Our forefathers have done much, but they have not finished anything." We of the present ephemeron must carry "from the alter of the past the fire and not the ashes," for the doctrines of surgery do not expire with each succeeding generation of surgeons.

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Surgical Technique

A NEW INSTRUMENT AND TECHNIQUE FOR COMMISSUROTOMY IN MITRAL STENOSIS

A. Nuñez Nuñez, M.D., G. Vazquez Rosales, M.D., and
J. Rodriguez-Iñigo, M.D., Havana, Cuba

(From the Department of Surgery of the University Hospital, Havana University)

IT IS well known that the surgery of mitral stenosis has recently been greatly advanced because of the work of Bailey,[1-4] Glover,[5, 6] Harken,[7, 8] and others.[9-15]

There are three features upon which this type of transmyocardial-palpation surgery is founded and which differentiate it basically from conventional surgery.[16] They are:

1. The surgeon is unable to see the structures upon which the operation is performed.

2. It is necessary to maintain the functional activity of the heart as a pumping unit. To achieve this purpose one must obtain and maintain a leak-proof closure of the incision upon the heart so that the loss of blood is not considerable.

3. The surgical maneuvers must be as simple as possible. Up to the present time these maneuvers have been limited to (a) exploration and diagnosis of intracardiac lesions; (b) commissurotomy by the finger-fracture method; (c) instrumental commissurotomy with any of the various instruments designed, all of which are introduced into the heart together with the exploratory finger; and (d) palpation after the surgical procedure has been performed in order to determine the adequacy of the commissurotomy and, if necessary, to continue or repeat the procedure.

The by-pass or bridge operation for the relief of mitral stenosis has given way to the method of direct attack on the stenosed mitral valve.

Since 1923, when Cutler for the first time sectioned a stenosed mitral valve, and up to the present time, several methods and techniques have been devised to section the mitral valve, but all except two have been abandoned. These two are: the instrumental commissurotomy, or Bailey's technique, and the finger fracture, or Harken's method. Commissurotomy, the section of the commissures or Bailey's method, is an instrumental operation, since the finger that carries the commissurotome is not in contact with the valve at the moment it is sectioned. The finger fracture, or Harken's method, is a purely digital operation.

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The Combined Method of Commissurotomy.—We agree that 80 per cent of the cases can be handled with the finger-fracture method, but we think that it is better to make a clean section of the commissures with the instrument guided by the right index finger in the atrium than to risk a wrong tear with its consequent regurgitation; so we have recently developed a combined method in which a commissurotome is introduced through the wall of the heart and, once inside the atrium, is guided by the right finger introduced through the auricular appendage in the usual manner.

The ideal section is at the exact line of fusion of the two valvular leaflets, and we believe this can be achieved by our combined digital and instrumental method.

Fig. 1.

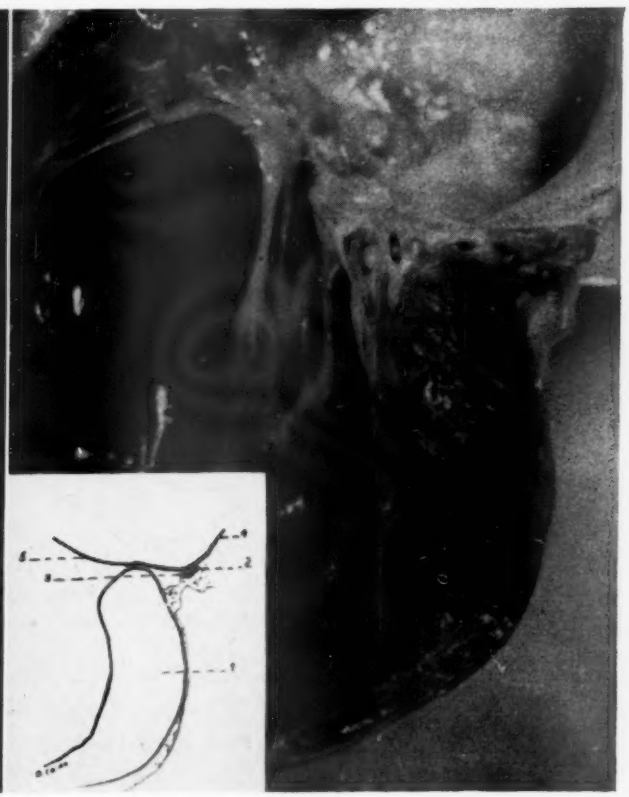

Fig. 2.

Fig. 1.—Longitudinal section of the left side of a normal heart at the level of the anterolateral commissure. Diagrammatic insert shows: *1*, ventricular wall; *2* and *3*, coronary vessels; *4*, atrial wall; *5*, atrioventricular ring.

Fig. 2.—Longitudinal section of left side of heart with mitral stenosis. The atrial wall is displaced outward together with the coronary vessels. Insert shows the same structures as in Fig. 1.

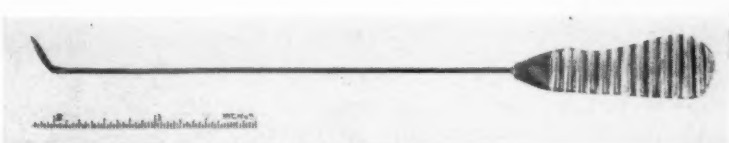

Fig. 3.—The commissurotome.

This method was developed after a thorough observation of the anatomy of autopsy specimens with mitral stenosis and was experimentally performed in fifteen dogs before being applied to human beings.

In a longitudinal section of the left side of the normal heart (Fig. 1) at the level of the anterolateral commissure, it may be observed that the upper extremity of the thick ventricular wall is rounded and convex. The outer surface is prolonged by the atrioventricular fat to where the coronary sinus and artery are located. On the inner surface the ventricular wall is continued by the thin atrial wall, and at the site of the union of the atrial and ventricular walls there is fibrous tissue called the atrioventricular ring where the mitral valve is inserted. In a longitudinal section of the left side of a heart with mitral stenosis it is observed that the atrial wall is displaced outward by the dilatation and that it carries with it the coronary artery and sinus, thus making it possible to palpate the convexity of the upper end of the ventricular wall, with the right index finger situated inside the left atrium (Fig. 2). This was observed in fourteen autopsy specimens of mitral stenosis.

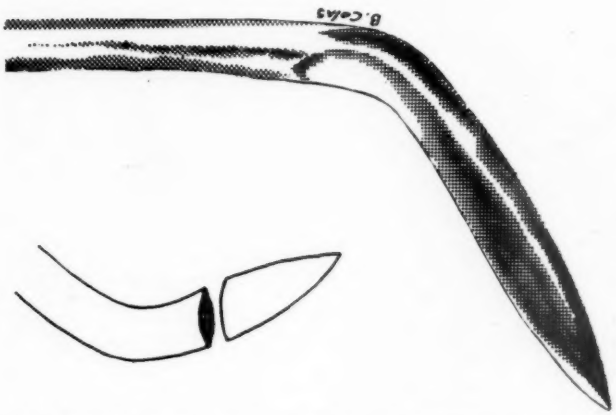

Fig. 4.—Detail of the sharpened segment of commissurotome.

The Commissurotome.—The instruments used in cardiac surgery must meet several requirements. They must either be flattened so that they can be introduced into the atrium together with the index finger, or rounded and of such small caliber that the injury produced by their insertion is similar to that produced by a puncture needle.

The commissurotome devised by us* consists of a cylindrical rod 12 cm. long and of the same caliber as an 18 gauge needle. The distal end is bent to an eighty-degree angle, and this angulated segment is flattened, leaving two cutting edges and a sharp point. The cutting edges point in the direction of the longitudinal axis of the instrument, and the handle has a concavity that indicates the position of the sharp point.

Technique for Commissurotomy (Figs. 5 and 6).—Through the regular approach, thoracotomy, the heart is exposed after the pericardium is opened. The index finger of the right hand is introduced into the left atrium through the auricular appendage in the usual manner. The stenosed valve is explored, and

*Manufactured by V. Mueller & Co., Chicago, Ill.

the anterolateral commissure is localized; this is located when the patient is in right lateral decubitus, in a position corresponding to eleven on the clock face. With the exploratory finger in the left atrium, one is able to palpate the upper end of the ventricular wall between the insertion of the mitral leaflet and the auricular wall. This is made possible by the dilatation of the left atrium bulging at the level of the atrioventricular sulcus, thus displacing the coronary vessels, although this event is not strictly necessary for performance of the operation. Two hemostatic U sutures are placed in the ventricular wall about 1 cm. apart, at

Fig. 5.

Fig. 6.

Fig. 5.—The right index finger in the left atrium palpates the upper end of the ventricular wall.

Fig. 6.—See text.

the point where the commissurotome is going to be introduced. The instrument is held with the left hand with the flattened end toward the ulnar side of the hand and the handle between the thumb and index finger. The sharp point must be pointing downward. The instrument is introduced, and at the same time a counterclockwise motion is made with it until the point is felt by the finger situated in the atrium. A further introduction places the whole angulated sharp segment inside the atrium with its point opposite to the mitral valve. A 180-degree rotation situates the point toward the valve, and with the right index finger the point is hooked in the stenosed orifice. Each of the cutting edges faces one of the commissures. The section is made with gentle movements of the in-

strument from the outside, pulling to cut the anterior commissure or pushing to section the posterior one, and is always guided by the right index finger inside the atrium. A new 180-degree rotation makes the sharp point face upward, and a gentle traction moving the instrument clockwise reverses the maneuver of introduction and brings it out. The hemostatic U sutures are crossed and tied, and new sutures are placed if necessary.

Up to this writing we have had six cases, with good functional results in five and one death due to cerebral embolism.

Fig. 7.—Arrow points to line of section in mitral valve on autopsy specimen of patient who died of cerebral embolism.

The instrument has also been introduced through the atrial wall, in one case in which the wall was not very dilated, with good results.

SUMMARY

A new combined method, instrumental and digital, for commissurotomy is presented. The instrument, designed by the author, and the anatomic bases for its use are described. A preliminary report of the results of the first six cases is included.

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Surgical History

CONDUCTED BY JOHN R. PAINE, M.D.

EPONYMIC FRACTURES: JOHN RHEA BARTON AND BARTON'S FRACTURES

LEONARD F. PELTIER, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, Division of Orthopedic Surgery, University of Minnesota Medical School)

> *I have directed your attention to Barton's work to show you that at the beginning of the nineteenth century there was already a native school of American surgery in which new operations were initiated and successfully carried out.* [Sir Arthur Keith.[10]]

A RECENT examination by the American Board of Orthopedic Surgery asked for a definition of Barton's fracture. Casual reference to the dictionary revealed that in addition to a Barton's fracture there was also a Barton's bandage and a Barton's bran dressing, but nothing else. While the names of Pott, Colles, and Bennett form integral parts of the tradition of British surgery, Barton, an American, is almost completely unknown to his own countrymen. It is only proper that the work of this great surgeon should be recalled, for by his own work and through that of his students John Rhea Barton played an important role in directing the growth and development of American surgery.

THE FRACTURE

What is Barton's fracture? It is "a separation fracture of the lower articular surface of the radius."[4] It is "a fracture of the distal end of the radius."[6] It is "a fracture of the lower articular end of the radius."[17] It is "a fracture-dislocation of the radio-carpal joint."[11] There is, in truth, "no such thing as a Barton's fracture."[8] Having assembled this "information," the question still remains: What is Barton's fracture? Rather than consult any more authorities, let us turn to the original description of the injury and see what Barton himself said.

In 1838, in an article entitled "Views and Treatment of an Important Injury of the Wrist,"[3] John Rhea Barton of Philadelphia presented the first account of the injury which has subsequently borne his name.

> The accidents which are to be the principal subject of my remarks, usually pass either for sprains or dislocations of the wrist.
>
> In simple sprains of the wrist, though accompanied by extreme swelling, the limb will still be found to retain a characteristic outline of its natural contour. It is not marked by any abrupt and solid eminences, the swelling is rather uniform, diffuse and puffy, the hand continues on the same line with that of the forearm, etc. In complete dislocations, the nature of the injury must always be very palpable from the great bulging of the overlapped bones and from the shortening

of the limb, etc. Between these two injuries there is too great a dissimilarity to admit of an excuse for the surgeon who mistakes the one for the other; but he may confound with these and it is a common fault to do so, *a subluxation of the wrist, consequent to a fracture through the articular surface of the carpal extremity of the radius;* although to this accident belong appearances exclusively its own. [The italics are Barton's.]

It is to this peculiar injury that I wish to draw attention. This accident must not be confounded with those which are also of frequent occurrence, namely, fractures of the radius, or of the radius and ulna, just above, and not involving the joint. [That is, Colles' fractures.]

The fragment may be, and usually is, quite small, and is broken from the end of the radius on the dorsal side, and through the cartilagenous face of it, and necessarily into the joint.

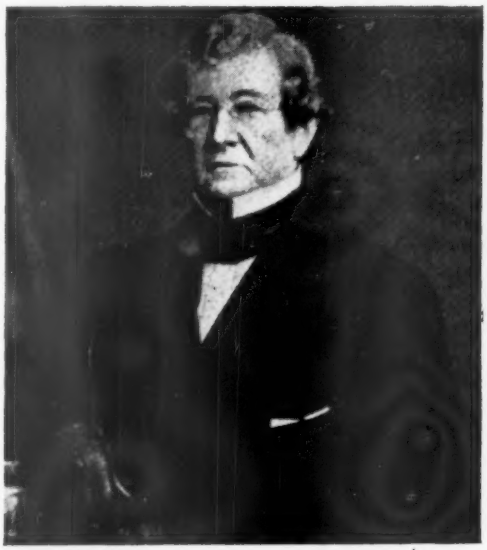

Fig. 1.—John Rhea Barton, photograph from the files of the Library of the College of Physicians of Philadelphia.

The only important change, which takes place in consequence of this fracture is, that the concave surface at the extremity of the radius, which receives and articulates with the three first carpal bones, is converted, as it were into an oblique surface by the loss of a portion of its marginal ridge; commonly by the separation of an entire piece, sometimes by the crushing of its substance. The moment the cartilagenous extremity of the radius is deprived of its concave form, the united force of the carpal and digital flexors and extensors is exerted to create a complete luxation; but, as the ligaments are only stretched, or but partially torn, this cannot take place. The carpal bones, therefore, only emerge collectively from their natural position, and carrying before them the broken piece, rest on the dorsal side of the radius forming a tumor there, whilst the end of the radius itself occasions on the palmar side a prominence which is round and smooth.

It sometimes happens also, though rarely, that fracture of a similar character to the one just described, occurs *on the palmar side* of the radius, from the application of force against the back of the hand whilst it is bent forward to its ultimate degree. Whenever the fracture takes place in front, the end of the radius projects over the wrist on the dorsal side, and the carpal bones and fragment rise out of their proper situations, and form the tumor on the palmar side thus reversing the deformity of the arm.

Barton considered fracture dislocation of the radiocarpal joint to be a rather frequent injury. This is not the case. Among 431 cases of fractures of the radius involving the wrist joint, Böhler[5] found only seven dorsal and eleven volar fracture dislocations of the radiocarpal joint. Some standard works on fractures make no mention of such injuries.

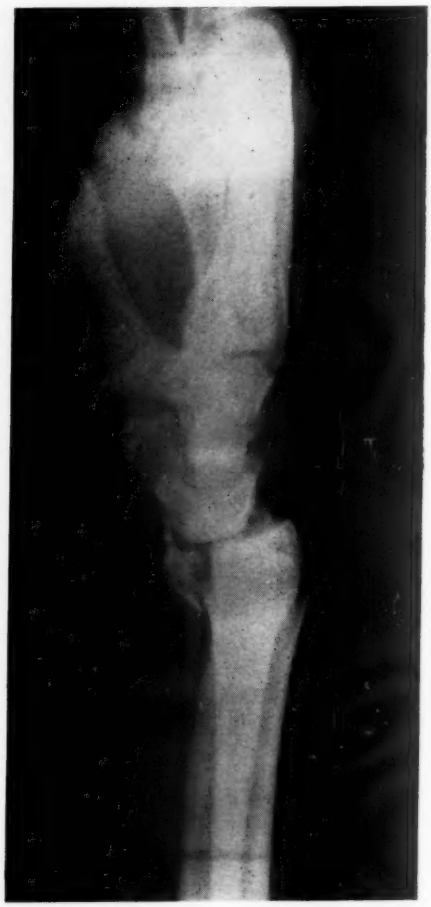

Fig. 2.—A case of Barton's fracture of the more frequent type from the practice of Dr. Harry B. Hall of Minneapolis.

Barton recognized the unstable nature of the reduction in fracture dislocations of the wrist, in contrast to the stable reduction obtained in simple dislocations. The displacement could easily be reduced by traction on the fingers with the elbow bent to a right angle, but when traction was released, the displacement recurred. For this reason, the arm was splinted while traction was carefully maintained. It was released only after the last bandage was tied in place. The dressing was examined frequently during the healing period to be certain that subluxation did not recur. The difficulty in preserving the reduction of these fracture dislocations persists to this day as a challenge to the ingenuity of the surgeon.

Stimson[18] felt that there were three good reasons to explain why this injury should not be known as Barton's fracture. First, the injury which Barton described clinically was not what he supposed it to be, but was the ordinary Colles' fracture. Second, the lesion he had supposed to exist had been observed some years before, and the specimen had been shown at one of the Paris societies. Third, the injury deserved to be classified, not as a variety of fracture, but as a dislocation of the wrist complicated by a fracture of the radius.

Stimson's objections can hardly be based on a first-hand knowledge of Barton's paper. Reference to the original description clearly demonstrates Barton's understanding of the anatomy involved in the injury. In addition, Barton specifically separated this injury from the common fracture of the distal end of the radius which does not disturb the relationship of the radiocarpal joint, that is, Colles' fracture. In 1839, one year after Barton's description, Voillemier,[19] discussing dislocations of the wrist, mentioned a case shown previously before a Paris society by Lenoir. This case, of which no details were presented, was referred to as a dislocation of the wrist accompanied by a fracture of the radius. One cannot grant Lenoir priority here on such a meager showing. Letenneur,[12] in 1839, confirmed Barton's description by presenting a case of volar dislocation of the wrist accompanied by a fracture of the anterior articular ridge of the radius. It is hard to suspect Barton of overlooking anatomic details of which others were becoming aware. From the accurate nature of his initial observation, it is obvious that he did not. Stimson referred to Shoemaker's[16] case as the first Barton's fracture to be diagnosed by x-ray picture. Examination of the illustrations shows that this case is not what Barton described, which leaves the impression that Stimson's knowledge of this injury was faulty. His only valid criticism seems to be the last. Barton's fracture should be considered a subluxation of the wrist with a fracture of the radius, in the same way that Bennett's fracture of the first metacarpal should be known as a fracture dislocation.

This fracture dislocation of the wrist received its eponym Barton's fracture in Hamilton's *A Practical Treatise on Fractures and Dislocations* published in Philadelphia in 1860.[7] This book has the distinction of being the first complete work on fractures and dislocations to be written in English. Hamilton,[13] who received his M.D. degree at the University of Pennsylvania in 1835, undoubtedly was acquainted with Barton and may have had his interest in fractures stimulated by this contact. At the University of Buffalo, where he became Professor of Surgery in 1847, Hamilton devoted a great deal of time to the evaluation of the end results of fracture treatment. He was also well known as a plastic surgeon, having performed the first crossleg pedicle graft in 1854. In 1868, after distinguished service in the Civil War, he was appointed Professor of Surgery at Bellevue Hospital, New York City. Dr. Hamilton and D. Hayes Agnew, another student of Barton's, shared the responsibility of caring for President Garfield after his assassination. William Halsted[9] was one of Hamilton's last interns at Bellevue and was greatly influenced by his attitude toward medical research. This contact led to several of Hal-

sted's early papers which dealt with methods of treating fractures by traction. There was a portion of Barton's highly original spiritin both of these surgeons.

THE MAN

John Rhea Barton could well be proud of his family. His father, Judge William Barton of Lancaster, Pa., was a distinguished lawyer, author, and among other things the designer of the United States Seal. His uncle, Benjamin Smith Barton, the well-known botanist, was the successor of Benjamin Rush as Professor of the Theory and Practice of Medicine at the University of Pennsylvania. His brother, William Paul Crillon Barton, made his mark both as a physician and as a medical administrator, holding the position of Professor of Materia Medica and Botany at Jefferson Medical College (1828 to 1830) and Chief, Bureau of Medicine and Surgery of the Navy Department (1842 to 1844). Small wonder, then, that John Rhea Barton himself was attracted to a career in medicine.

Barton received his medical education at the University of Pennsylvania, graduating from the Medical Department in 1818 at the age of 22 years. The title of his thesis, "Certain Injuries of the Bones of Children," would indicate that his interest in fractures was already manifest. Two years later he was appointed one of the surgeons to the Philadelphia General Hospital. From 1823 to 1836 he was a member of the staff of the Pennsylvania Hospital. He retired from active practice in 1840.

During his five-year apprenticeship in the Pennsylvania Hospital (1813 to 1818), he had as his teachers and mentors two most distinguished American surgeons, Phillip Syng Physick and his nephew, Phillip Syng Dorsey. Physick, the "father of American surgery," had been the student and intimate of John Hunter. He returned from England imbued with Hunter's spirit and transfused it liberally into his pupils. Physick himself devised many improvements in the apparatus used to treat fractures of the femur, but his most celebrated innovation was the use of the seton in the treatment of ununited fractures. One would not be far wrong in assuming that Barton's subsequent development stemmed at least in part from this intellectual milieu which was Hunter's legacy to America.

John Syng Dorsey, as Physick's nephew, was educated under his especial care. He was sent to England to polish off his training. There he became acquainted with Everard Home, Hunter's professional executor, and Sir Astley Cooper, another alumnus of Hunter's exclusive little "college" and the most outstanding surgeon of his time. Dorsey was a consummate technician, a brilliant operator. His career was cut short by untimely death at the age of 35, but not before his striking personality had had its effect upon Barton.

In his practice Barton became known for his ingenuity in adapting mechanical principles to problems of fracture treatment. He devised a figure-of-eight bandage of the head to be used in the treatment of fractures of the mandible (Barton's bandage). He introduced the use of bran as an absorbent material to take up the drainage from compound fractures of the leg.

For an elucidation of the more personal aspects of his nature I prefer to quote at length from a speech given by Dr. D. Hayes Agnew at the commencement exercises of the Medical Department of the University of Pennsylvania in 1878 after Barton's death.

> The biographical artist, in portraying the life of his hero, loves to dwell chiefly on those events or achievements which have attracted public admiration, too often forgetting the numerous though less conspicuous characteristics which not only serve to consolidate the character and lead to great success, but also, from the multiform points in which they come in contact with our humanity, confer extraordinary grace on the life. The glory of the Alps does not wholly consist in the mighty mountain peaks which send their spires into heaven, clothed with sunshine and cloud; a thousand charms are seen in the little foothills, the grassy vales, and the rippling streams which catch the eye of the pleasure-seeking tourist. And so with the subject of our sketch: it was not alone those achievements that bear the stamp of originality which heralded his fame on the wings of the wind and made his name a tower of strength, but there were other charms of social and professional life which have rendered his memory fresh and fragrant in the hearts of his friends.
>
> As an operator, Dr. Barton was cool, decided, elegant, and full of resource. Using either hand with equal facility, he seldom changed his position when engaged in any surgical procedure. His dressings were applied with the utmost precision and neatness of detail. The roller with him was like plastic clay in the hand of the potter; obedient to the master's wish, every turn fell into place like a well-fitting garment; indeed, there was an unstudied grace in every movement of the man.
>
> With an easy dignity of manner, a cheerful disposition, and a heart full of human kindness, he possessed in a remarkable degree the quality of personal magnetism, inspiring all who came within the limits of attraction with an enthusiastic admiration for the profession which he adorned. It was entirely through his influence, unconsciously exerted, that our good and distinguished friend Prof. Francis Gurney Smith was led to the study of medicine.
>
> In his daily walk through the wards of the hospital he never failed, as he passed from bed to bed, to drop a kind word of encouragement, which, joined to his sympathetic manner, acted like a cordial upon the drooping spirits of the sufferers under his care.
>
> With all his other qualities of head and heart, Barton was a man of great simplicity of life, and entirely free from all appearance of ostentation or display. He moved quietly among his fellow-townsmen without drumbeat or flaunting banners. I remember well his equipage. Not a showy phaeton drawn by fiery steeds whose pedigree might be traced to the stalls of Solomon; no buttons, no tigers, no obsequious lackeys to herald the presence of the man, but a plain, substantial horse and buggy, driven by those hands whose cunning had wrought so many marvels of surgical skill.
>
> The sun sinks below the western horizon, but long after the great body of flame has passed out of sight there lingers on the bending sky a mellow sheen of golden glory; and so men die and drop out of rank, but the influence and power of their lives remain the heritage of succeeding generations.

THE SURGEON

To delineate the character of Barton's surgical achievement, let us review the record of several of his more interesting cases.

On Aug. 18, 1824, a sailor was admitted to the Pennsylvania Hospital with a fracture of the spine, caused by a fall from the masthead of a brig. The lower

part of the trunk and the lower extremities were paralyzed. He was incontinent of urine and feces. His condition remained unchanged. Two weeks later Barton exposed the injured area through an incision about eight inches long. The spinous process and the lamina of the seventh dorsal vertebra were broken off and were compressing the cord. After removing these fragments he found that there was a dislocation of the seventh vertebra upon the eighth. The wound was then dressed with lint. Forty-eight hours later sensibility began to return below the level of the injury and gradually extended toward the toes. On the third postoperative day the patient was seized by a violent chill and died twelve hours later. Examination of the spine confirmed the findings at operation and in addition revealed extensive hemorrhage into the substance of the cord.[14]

Laminectomy for paraplegia following fractures of the spine was discussed by Paul of Aegina in the seventh century, and again by Paré in the seventeenth. Chopart and Desault spoke of it as a simple procedure. Sir Astley Cooper had assisted his teacher, Mr. Henry Cline, in such an operation, this case also ending fatally. Nevertheless, although widely discussed, such operations were of rare occurrence. This operation, performed early in his career, already marked Barton as a surgeon of uncommon boldness and resource.

J. C., a 21-year-old sailor, presented himself to Barton in October, 1825, seeking aid. Six months before, he had injured the right hip in an accident aboard ship. He had been unable to walk since. The hip was firmly fixed in adduction, internal rotation, and almost ninety degrees of flexion. It did not appear to have been dislocated. Barton first applied traction to the limb over a period of a few weeks, but was unable to change the position. During a whole year the patient remained in the hospital without improvement. This was not time wasted, for to Barton he was a persistent challenge, an unsolved problem. Finally, after long preparation, the problem was solved in a masterful manner.[1]

On Nov. 22, 1826, in a public operation attended by a large number of students and visiting physicians, Barton exposed the lateral border of the upper end of the femur, and using a saw, especially made for this operation, divided the femur just above the lesser trochanter. This allowed the deformity to be corrected. The wound was dressed with lint and adhesive straps. The procedure lasted seven minutes and was borne with great fortitude by the patient. The wound healed by secondary intention with only one episode of erysipelas. As soon as the wound appeared to be healing satisfactorily the leg was put through a gradually increasing range of motion with the intent of producing non-union and a pseudoarthrosis. The attempt was successful, and soon the patient was able to bear weight. The pseudoarthrosis was a stable one and had a fair range of motion, and there appeared to be only one-half inch of measurable shortening of the limb. The patient left the hospital walking without aid, and soon established a shop as a basketmaker, able once again to support himself and his family. A satisfactory range of motion persisted in the right hip for six years after which, associated with a general decline in health, stiffening gradually occurred, although in a useful position.

Some time later the patient succumbed to pulmonary tuberculosis. Barton had obtained the consent of the patient to remove the specimen after his death. This he did, and the dissection revealed a typical pseudoarthrosis with fibrous ankylosis.

Barton had artfully produced a pseudoarthrosis as close to the joint as possible. He wrote,[1] "I did believe, that nature would not passively witness my labours to effect what she has so often herself endeavored, unaided by art, to accomplish; but that she would be ready to cooperate with me, and to extend to completion, that which human art alone would be incapable of."

This operation was the first arthroplasty. From the title of his article, "On the Treatment of Anchylosis by the Formation of False Joints," it can be seen that Barton clearly understood that he was not performing a simple osteotomy. Reference to his illustration shows that he felt it possible to perform arthroplasty in other joints. The indications for arthroplasty which he outlined in 1827[1] apply today.

> I hope that I will not be understood as entertaining the belief, that this treatment will be applicable to, and judicious in, every case of anchylosis. I believe the operation would be justifiable *only* under the following circumstances, viz. Where the patient's general health is good, and his constitution sufficiently strong; where the rigidity is not confined to the soft parts, but is actually occasioned by a consolidation of the joint; where all the muscles and tendons, that were essential to the ordinary movements of the former joint, are sound, and not incorporated by firm adhesions with the adjacent structure; where the disease, causing the deformity, has entirely subsided; where the operation can be performed through the original point of motion, or so near to it, that the use of most of the tendons and muscles will not be lost; and, finally, where the deformity, or inconvenience is such, as will induce the patient to endure the pain and incur the risks of an operation.

This concept of forming false joints, or arthroplasty, is Barton's most important contribution to surgery. Although he performed only one such operation, the discussion accompanying his case report formulated the fundamental principles of arthroplasty, which are accepted to this day.

In 1834, dissatisfied with the prevailing methods of treating fractures of the patella, Barton performed an open operation in such a case and sutured the fragments together with a wire passed through the fragments and knotted outside the skin.[18] The patient died as a result of the sepsis, which shortly ensued. Patellar suture was not practical until after the perfection of antiseptic surgery by Lister, who, appropriately enough, reintroduced the technique successfully.

A year prior to his last major publication, "Views and Treatment of an Important Injury of the Wrist" (1838),[3] Barton described another approach to the problem of joint disease, "A New Treatment in a Case of Anchylosis."[2] In this instance the patient was a physician with an ankylosis of the knee in marked flexion. This was the result of a suppurative arthritis occurring many years previously. The deformity was such as to cause almost total disability. Barton exposed the supracondylar portion of the femur by means of an incision above the patella. Using a saw, a wedge of bone was removed from the femur, leaving a portion of the posterior cortex of the femur intact. The

wound was dressed with lint, and slowly healed by secondary intention. As the wound healed, the knee was slowly extended by means of an adjustable splint and by moderate traction. Three months after the osteotomy, the wound was well healed and the bone had united with the knee in almost complete extension. The end result was a limb with a knee joint stiffened in a good functional position. The physician returned to active practice.

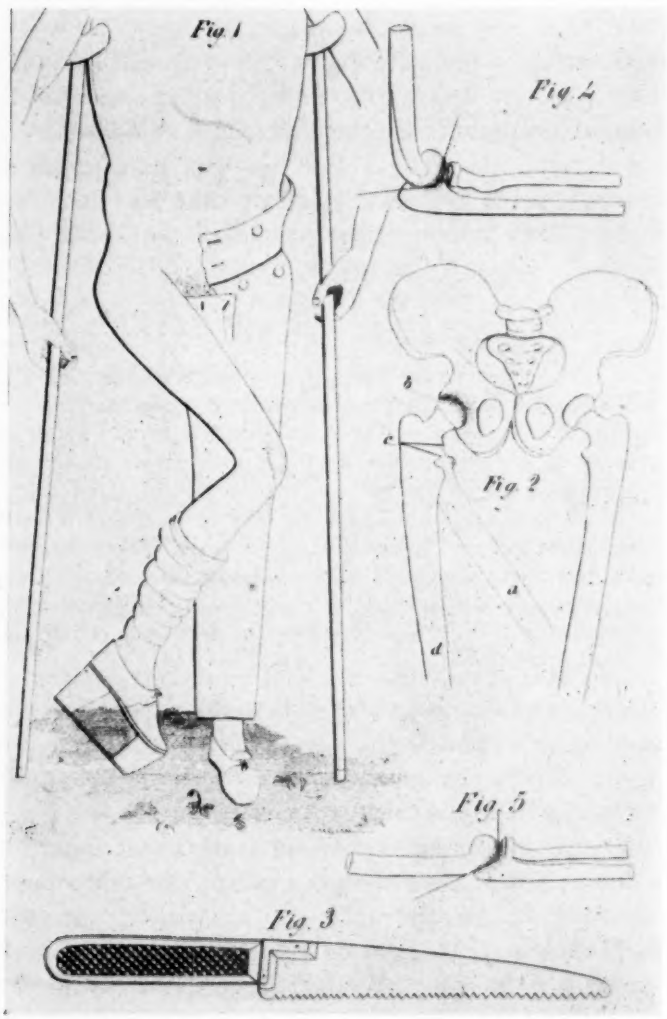

Fig. 3.—Figures illustrating the case of J. C. and showing details of the first arthroplasty. The proposed method of arthroplasty in cases of ankylosis of the elbow is also shown.[1]

These few examples of Barton's originality, daring, and technical resource are even more remarkable when we consider that they were carried out prior to the discovery of anesthesia and antisepsis.

BARTON'S LEGACY

Fortunately for us, Barton's contribution to the development of surgery in America did not end with his death. The minutes of the Board of Trustees of the University of Pennsylvania for Nov. 6, 1877, contain the following notation:

"Mrs. John Rhea Barton gave $50,000, the income thereof to be annually forever appropriated to the payment of the salary of a Professor of Surgery who shall be the occupant of a chair to be designated as the John Rhea Barton Chair of Surgery." This represented the first full and permanent endowment of a medical professorship in this country.[15]

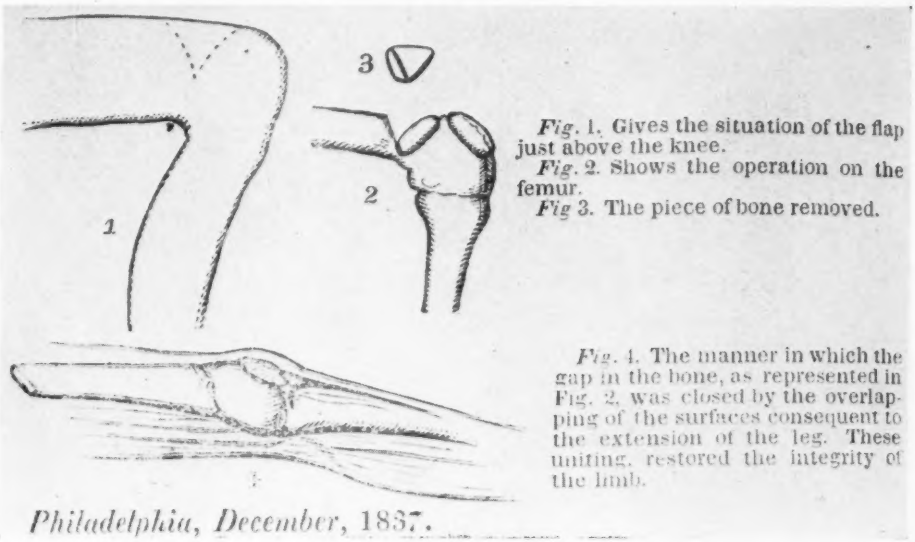
3
2
1
Fig. 1. Gives the situation of the flap just above the knee.
Fig. 2. Shows the operation on the femur.
Fig 3. The piece of bone removed.
Fig. 4. The manner in which the gap in the bone, as represented in Fig. 2, was closed by the overlapping of the surfaces consequent to the extension of the leg. These uniting, restored the integrity of the limb.
Philadelphia, December, 1837.

Fig. 4.—Figures illustrating the treatment of a limb with the knee ankylosed in flexion by means of supracondylar osteotomy.[2]

This gift was formally acknowledged by D. Hayes Agnew, the first occupant of the new chair, in an address, a portion of which has been quoted earlier. Barton's name and spirit have continued to live in the persons of the distinguished surgeons who have held the title, John Rhea Barton Professor of the Principles and Practice of Surgery. This is not the place to discuss the contributions of these men. However, an examination of their names will emphasize the important role which this chair of surgery has played and is playing in the American surgical scene.

D. Hayes Agnew	1877 to 1889*
John Ashurst, Jr.	1889 to 1900
J. William White	1900 to 1911
Edward Martin	1911 to 1918
John B. Deaver	1918 to 1922
Charles H. Frazier	1922 to 1936
Eldridge L. Eliason	1936 to 1945
I. S. Ravdin	1945 to date

CONCLUSION

Barton's fame rests today not on his bandage, his bran box, or even on his fracture. It rests on his conception and execution of the first successful arthroplasty and his pioneer work on osteotomy for the correction of deformity. These operations are a part of the basic armamentarium of the surgeon en-

*Tenure as John Rhea Barton Professor of Surgery, University of Pennsylvania.

gaged in reconstructive surgery. Among his students were several who were influenced by the stimulus of his example and who, by emulation, made great contributions to surgery. No finer monument to his name could exist than the John Rhea Barton Chair of Surgery, whose occupants have exercised great influence on the development of surgery. It is time to rescue Barton's career from the obscurity which has cloaked it and to recognize him for what he was, one of the founders of a great tradition in American surgery.

Acknowledgments.—Dr. I. S. Ravdin, the present John Rhea Barton Professor of Surgery, University of Pennsylvania, was of great assistance in gathering material. Dr. Ravdin's contributions to American surgery make him especially fitted to bear the eponym of his distinguished predecessor. The author also wishes to express his appreciation of help furnished by W. B. McDaniel, II, Librarian of the College of Physicians of Philadelphia.

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